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## METASTASIS OF NEOPLASMS TO THE CENTRAL NERVOUS SYSTEM AND MENINGES

STANLEY LESSE, M.D.

AND

MARTIN G. NETSKY, M.D.

NEW YORK

THERE ARE few reports of metastatic neoplasms in the central nervous system and meninges based on study of a large series of complete necropsies. An unusually large number of such examinations on patients with cancer was available at Montefiore Hospital. An analysis of the findings in this group is presented.

### MATERIAL

During the period from 1938 to 1947, there were 595 complete necropsies performed upon patients who died with cancer. In all these instances the brain was examined, but the spinal cord was studied in only 76 cases. Cases without cancer and those in which examination of the central nervous system was not performed were excluded from consideration in this paper. Metastatic lesions in the central nervous system or meninges were found in 207 cases (35% of the total of 595 necropsies).

The primary and metastatic tumors were studied with hematoxylin and eosin preparations in all cases. Special stains, including the Sudan, phosphotungstic acid-hematoxylin, Masson, and Wilder techniques, were employed when deemed appropriate. The cerebral tissue surrounding the metastases was further studied in certain cases by the methods of Nissl, Spielmeier, Cajal, and Weil.

### INCIDENCE

Figures cited in various reports concerning the incidence of metastatic tumors are strongly altered by factors of selection. Some of these factors are considered in more detail under "Comment." The incidence of metastatic neoplasms may be considered in two ways. The first deals with the frequency of metastases to the neuraxis in relation to the incidence of systemic cancer. In how many patients with cancer will there be metastases to the nervous system or meninges? In most large series of necropsies (Table 1) metastases to the brain are reported as occurring in from 2 to 6% of cases. The occurrence of metastases to the neuraxis in more than one-third of the necropsies in the present series is unusual, but the fact is in accord with the finding of widespread visceral dissemination previously reported from this institution.<sup>7</sup>

The second type of incidence deals with the frequency of metastases in relation to the incidence of other intracranial tumors. This type presents the more pertinent clinical problem of how often cerebral or spinal metastatic tumors occur in patients with signs and symptoms of neoplasms in the neuraxis. These figures also vary greatly in selected populations. A study based on neurosurgical patients probably

From the Laboratory, Neuropsychiatric and Neoplastic Divisions, Montefiore Hospital.

will result in too low a figure because of reluctance to explore a patient with known cancer and because of the rapidity of the course in such patients when cerebral signs develop. In series which are predominantly neurosurgical, metastases form about 5% of intracranial neoplasms. This contrasts with the 10 to 30% noted in studies of necropsy material.\* The figure obtained here, of 58% (207 metastatic, 147 primary tumors), is the result of highly selective factors. During much of the decade covered in this study there was relatively little activity in the neurosurgical sphere. This factor is reflected in a decrease in numbers of primary brain tumors.

## CLINICAL DATA

*A. Age Incidence.*—The majority of patients with metastases were in their middle 40's. The youngest patient was 4½ years old (adrenal tumor) and the oldest 76 (mammary carcinoma). There was a difference between men and women in the age at onset of the primary lesion. The mean age of onset in the 124 female patients with metastases was 44 years, as compared with a mean age of

TABLE 1.—Comparison of Percentages and Sources of Neuraxial Metastases

Author	No. of Necropsies	No. of Metastases	Percentage of Metastases	Principal Sources of Metastases
1. Krastig (1906) <sup>1</sup> .....	985	53	5.7%	Breast, 10; uterus, 4; esophagus, 4; skin, 4; prostate, 4; lymphosarcoma, 3; lung, 0
2. Rau (1922) <sup>2</sup> .....	851	28	3.3	Breast, 7; lung, 7; stomach, 3
3. Neustaedter (1944) <sup>3</sup> .....	6,761	143	2.2	Breast, 14; lung, 8; pharynx and larynx, 8; tongue, 4
4. Baker (1942) <sup>4</sup> .....	...	115	...	Breast, 24; lung, 24; skin, 9; kidney, 9; adrenal, 6
5. Courville (1945) <sup>5</sup> .....	...	115	...	Lung, 39; breast, 12; liver, 4; skin, 4
6. Willis (1948) <sup>6</sup> .....	500	29	5.8	Lung, 9; breast, 7; kidney, 3; esophagus, 2; melanoma, 2
7. Lesse and Netsky (1953)....	585	207	34.8	Breast, 71; lung, 50; lymphoma, 13; kidney, 10

\* The fourth and fifth papers are reports of general autopsy series; the others deal only with necropsied cases of cancer.

47 in the 83 male patients. For many sources of metastases the mean age of onset in women was 5 to 10 years earlier than that in men. Figure 1 shows the age of onset in decades for 191 cases of neuraxial metastases and demonstrates that metastasizing tumors, as a whole, occur earlier in life than the majority of primary neoplasms. The variability of the ratio of the number of primary tumors to the number of metastases in the different decades is well shown.

The average age of onset is comparable in most reports, occurring in the middle of the fifth decade. The earlier onset of metastases in women is recorded by Neustaedter,<sup>3</sup> who found a peak of incidence in men in the sixth decade and in women in the fifth decade.

*B. Sex Incidence.*—There were 124 women and 83 men, a ratio of 1.5 to 1. The higher incidence in women is explained by the large number of patients in this series with carcinoma of the breast. In most reported series there is a slight predominance of males, which is related to a relatively greater frequency of primary bronchogenic neoplasms.† Usually, if there is a striking sexual difference, a male predominance

\* References 8 and 9.

† References 10 and 11.

# METASTASIS OF NEOPLASMS TO C.N.S. AND MENINGES

is found.† The series reported by Globus and Meltzer<sup>8</sup> contained only one patient with carcinoma of the breast.

In the present series the sex incidence in patients with metastases from primary cancer of the lung was strikingly different from the average. There were 33 males and 17 females (2 to 1). Despite the fact that there were more men in this group, the proportion of women was unusually high because the 229 patients with primary carcinoma of the lung were divided in a ratio of 3.4 males to 1 female. Although men predominated in both groups, pulmonary neoplasms in women metastasized to the neuraxis relatively more frequently than those in men. This finding may be explained partially by the fact that adenocarcinomas are commoner in women, but

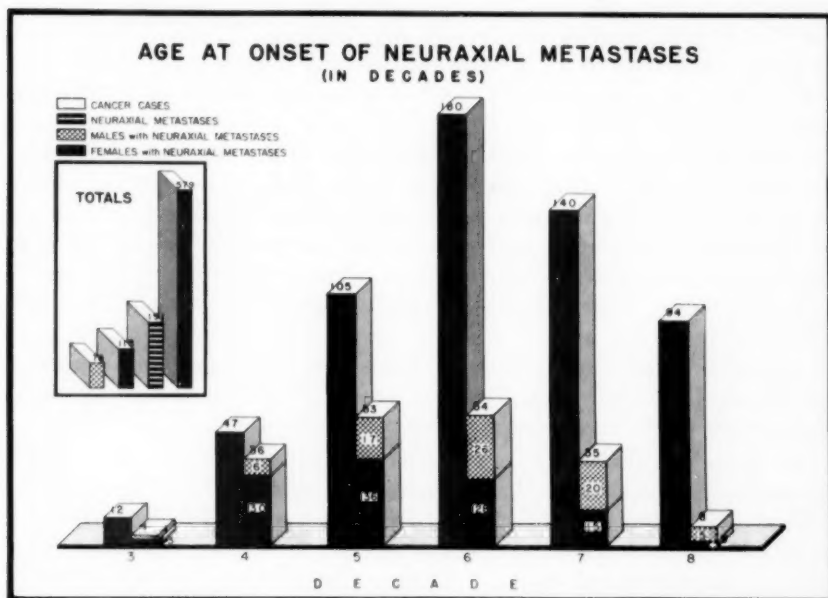


Fig. 1.—Incidence of cancer cases and of metastases by decade and by sex. The inset shows the totals for all decades. The earlier peak incidence of metastases in women and the lower rate of metastasis in the later decade are notable.

squamous cell carcinomas occur more frequently in men. The adenocarcinomatous type of pulmonary neoplasm may metastasize more frequently to distant sites.

*C. Interval Between Clinical Onset of Primary and Secondary Growths.*—In most patients this interval was slightly more than a year. In some instances, however, the central nervous system metastases were the first evidence of neoplasia in the patient. This was observed in 20 patients (10%). At the other extreme, a patient with cancer of the breast had an interval of 16 years between the onset of primary cancer and the clinical signs of its presence in the nervous system.

A comparison of patients having mammary cancer with those having pulmonary tumors revealed a striking difference. The average interval between the known

† References 8 and 9.



onset of carcinoma of the breast and evidence of a lesion in the neuraxis was 17 months, but with pulmonary tumors the average interval was only 5 months. There were four patients, all but one with cancer of the breast, who had intervals of 16, 14, 13, and 11 years, respectively, but the greatest interval in cases of carcinoma of the lung was 2½ years.

There were 67 patients (32%) with asymptomatic neuraxial metastases. More than three-quarters of the pulmonary metastatic tumors were symptomatic, but only about one-half of the cases of mammary carcinoma produced symptoms. The majority of leukemic infiltrations were asymptomatic. Absence of symptoms was commoner with dural metastases but occurred in patients with intracerebral lesions. Within the asymptomatic group there were three unusual patients, one with a primary cancer in the stomach who lived 13 years after the discovery of the primary neoplasm; another, who lived 12 years (primary in breast), and still another, who lived 11 years (primary in thyroid), all harboring silent intracranial neoplasms at death.

*D. Duration of Life after Onset of Clinical Signs of Metastases to the Neuraxis.*—Patients having tumors originating in the breast (71 cases) survived an average of five months, as compared with patients with pulmonary neoplasms (50 cases), who survived an average of three months. Patients who died with leukemia or malignant lymphomas survived approximately six months after the onset of neural involvement. Limitations of available data prevented evaluation of the remaining tumor groups.

In unusual instances survival after the onset of central nervous system symptoms was prolonged up to four years. Typically, however, the patient who develops signs of metastases to the neuraxis survives only a few months.

*E. Neurologic Findings.*—The following discussion deals only with the 128 patients having symptoms or signs of neurologic disease. Of these, 85 had intracerebral and/or meningeal involvement, and there were 43 with only meningeal metastases. The findings are summarized in Table 2. Striking differences in the effect of parenchymal and meningeal lesions are noted. There were 24 patients in whom the onset was rapid, within a period up to 48 hours. In 5 of these 24 it was apoplectic in nature. The onset was gradual in the remaining 104 patients, full development occurring only after many days or weeks. This was true in patients with parenchymal, as well as with meningeal, neoplasms.

There was no definite clinical pattern that differentiated metastatic from primary neoplasms. Unless the primary site of the neoplasm was evident before the onset of neurologic symptoms and signs, the differential diagnosis was difficult. Symptoms and signs occurred in 76% of the patients with parenchymal lesions, but in 52% of the patients with only meningeal lesions.

The commonest subjective alterations were headaches, personality and intellectual changes, and weakness. There were 38 patients in whom headache was a prominent symptom, and only 7 of these had meningeal neoplasms. The headaches usually were generalized, except in the presence of posterior fossa metastases, in which instance suboccipital pain was common. Headache was frequently an early symptom and sometimes was unrelated to increased intracranial pressure.



# METASTASIS OF NEOPLASMS TO C.N.S. AND MENINGES

Personality and intellectual changes also occurred in only 5 patients with meningeal metastases but in 36 with parenchymal metastases. Pyramidal tract signs and seizures were also commoner in patients with parenchymal tumors. Aphasia occurred

TABLE 2.—*Signs and Symptoms of Neuraxial Involvement (128 Cases)*

	Central Nervous System Lesions (86 Cases)	Meningeal Lesions (43 Cases)
Mode of onset		
Sudden .....	19	5
Gradual .....	66	28
Headache .....	31	7
Meningeal irritation.....	0	1
Mental and/or personality changes.....	28	5
Motor signs		
Hemiplegia .....	33	4
Monoplegia .....	4	4
Paraplegia .....	13	9
Pyramidal tract signs.....	46	4
Coma .....	5	2
Convulsions		
Grand mal .....	2	1
Focal .....	13	2
Extrapyramidal signs .....	0	0
Aphasia		
Expressive .....	11	0
Receptive .....	5	1
Ataxia .....	9	1
Vertigo .....	2	0
Cranial nerves		
I .....	0	0
II		
Papilledema .....	14	5
Scotomata .....	2	0
Hemianopsia .....	4	0
III, IV, VI		
Diplopia .....	5	4
Ophthalmoplegias .....	9	4
V		
Sensory .....	3	4
Motor .....	2	0
VII		
Central .....	15	5
Peripheral .....	2	5
VIII .....	0	2
IX, X .....	4	3
XI .....	1	0
XII		
Central .....	10	3
Peripheral .....	0	1

only in patients with central nervous system involvement. Extrapyramidal signs were not found in any patient, although the basal ganglions were invaded in 29 cases.

Cranial Nerves: Signs of implication of cranial nerves occurred in the following manner:

I. The olfactory nerves were not implicated in any case.

II. Some degree of papilledema was found in 19 patients, 14 with parenchymal lesions and 5 with meningeal lesions. This incidence represents only 15% of the total number of cases. Visual field defects were noted in six patients, all of whom had cerebral neoplasms.

III, IV, and VI. The commonest extraocular muscle involvement was sixth nerve paralysis, usually associated with increased intracranial pressure. In some cases of metastatic tumor these signs were the result of brain stem compression or invasion, or implication of the nerves at the base of the skull. External ophthalmoplegia of some type was found in 13 patients. Pupillary alterations were uncommon, usually being found in patients with striking increase in intracranial pressure or as a terminal phenomenon.

V. The sensory component of the fifth nerve was implicated in eight patients. Four of these patients had brain stem lesions, and four suffered from compression of the nerve by meningeal masses. The motor branch was affected in only one patient, in whom the brain stem was invaded by tumor.

VII. Supranuclear facial paralysis was found in many patients with hemiplegia or with increased intracranial pressure. Peripheral facial nerve paralysis was found in seven patients, five with meningeal tumors and two with neoplasms in the brain stem.

VIII. Hearing defects that could be ascribed to intracranial metastases were found in only two patients. There was no evidence of vestibular nerve involvement other than the complaints of vertigo found in many ill patients.

IX, X, XI, and XII. Only three patients had evidence of involvement of the lower group of cranial nerves. All three had intrinsic brain stem lesions.

There was evidence of meningeal irritation in only one patient, despite the fact that there were numerous patients with focal or diffuse meningeal metastases. This has been commented on by others.<sup>§</sup>

**Sensory Changes:** Relatively few patients had marked sensory abnormalities. A hemisensory deficit was noted in 15 patients in conjunction with hemiplegia. One patient with spinal meningeal involvement had a Brown-Séquard syndrome, while nine had clinical and anatomical evidence of cauda equina involvement due to meningeal lesions. In none of these cases were any segmental sensory deficits noted in the upper extremities.

**Reflexes:** Fifty patients had hyperreflexia and signs referable to the pyramidal tracts, 46 of these patients having intramedullary neoplasms, while only 4 had meningeal lesions only.

**Motor Signs:** Nine patients with spinal meningeal tumors, all in the cauda equina, showed definite segmental motor deficits, due to root compression. The incidence of weakness of the various extremities is shown in Table 2. It was a common finding that hemipareses would wax and wane in intensity before becoming progressive in the later stages of the disease. Nine patients with cerebellar lesions had marked ataxia.

**F. Diagnostic Accuracy.**—The diagnostic problems here were simpler than in most series because usually the existence of a primary lesion was known. In 195 cases there were sufficient clinical data upon which to base conclusions. In 87

§ References 8 and 12.

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(45%) of the 195 cases metastatic tumor was not diagnosed, in 67 because the central nervous system and meningeal lesions were asymptomatic, and in only 20 was the diagnosis incorrect. One hundred twenty-six patients presented neurologic signs or symptoms, and in 106 of these (84%) the signs were correctly diagnosed.

### ANATOMIC AND PATHOLOGIC DATA

*A. Sources of the Tumors.*—The breast and lung were by far the commonest sources, accounting for more than one-half of the 207 patients with neuraxial metastases. This finding is illustrated in Figure 2, which also demonstrates the other sources of metastases.

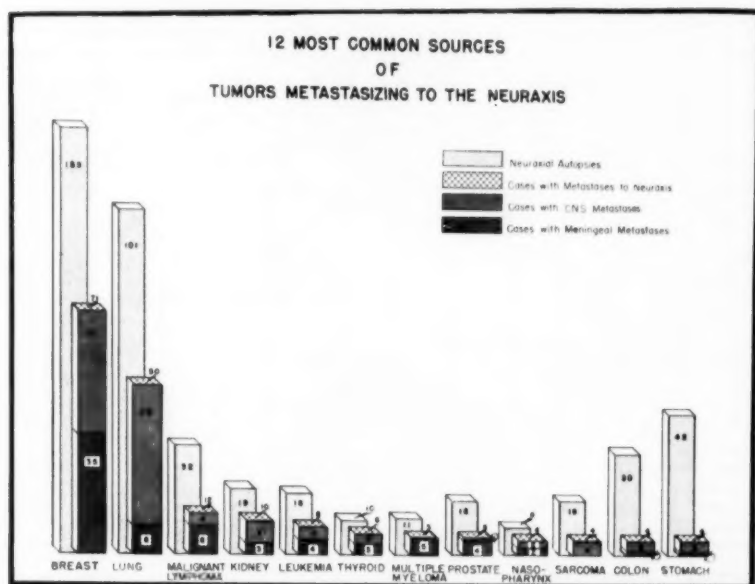


Fig. 2.—Total number of autopsies and number of metastases to the central nervous system and to the meninges for the 12 commonest metastasizing neoplasms. See text for further discussion.

The relation of brain metastases to the incidence of primary growths is interesting. Despite the common occurrence of gastrointestinal malignant growth (stomach, colon, rectum), they metastasize infrequently to the nervous system. They constituted 17% of the primary growths, but only 5% of the neuraxial metastases. Carcinomas of the esophagus, small intestine, pancreas, and ovary did not metastasize to the central nervous system in any instance in this series, although rarely they may do so. Tumors of the genitourinary system, with the exception of the prostate and kidney, metastasize infrequently. Tumors of the breast, lung, and kidney, on the other hand, often metastasize to the neuraxis. They represented 41% of the primary tumors, but 64% of the metastases were from these sources. Figure 2 graphically illustrates these facts for the 12 commonest types of tumor. The relative

incidence of cerebral metastases arising from most organs is higher in this series than in many others, but this incidence is related to the generally higher percentages of metastases encountered.

In Table 3 a comparison of various large necropsy series is made to determine the tendency for various primary cancers to metastasize to the nervous system. The absence of cerebral metastases of pulmonary cancer in the Krasting<sup>1</sup> report is difficult to accept, and perhaps some of these metastases were diagnosed as sarcomas. The percentage of metastases from various organs is generally similar in all four studies except that our figures are higher. Thyroid metastases are unusually high in the present series, as are the lymphomas. The metastasis of malignant lymphomas to the brain is considered in detail in another publication from this laboratory.<sup>13</sup>

TABLE 3.—*Metastasis to the Neuraxis of Various Primary Neoplasms\**

Primary Source	Krasting 935 Cancer Cases			Rau 851 Cancer Cases			Willis 500 Cancer Cases			Lesse and Netsky 595 Cancer Cases		
	Metas- tasis			Metas- tasis			Metas- tasis			Metas- tasis		
	Cases, No. of	No.	%	Cases, No. of	No.	%	Cases, No. of	No.	%	Cases, No. of	No.	%
Nasopharynx	8	2	25	..	..	..	61	1	2	8	4	50
Esophagus	74	4	5	57	1	2	17	2	12	10	0	0
Stomach	227	0	0	255	3	1	85	1	1	42	4	10
Colon	18	0	0	35	0	0	65	1	3	30	4	13
Rectum	44	1	2	44	1	2	Included in colon			31	3	10
Gall bladder	37	2	5	38	2	5	18	1	6	6	1	17
Liver	11	0	0	6	0	0	Included in gall bladder			3	1	33
Pancreas	15	0	0	19	0	0	11	0	0	10	0	0
Breast	53	10	19	36	7	19	45	14	31	125	71	57
Uterus and cervix	116	4	4	58	0	0	30	0	0	19	3	16
Ovary	29	0	0	7	0	0	9	0	0	24	0	0
Prostate	18	4	22	23	2	9	15	2	13	16	5	31
Kidney	23	2	9	9	1	11	10	3	30	19	10	53
Lung	14	0	0	30	3	10	27	9	33	101	50	50
Thyroid	23	2	9	6	0	0	6	0	0	10	6	60
Sarcoma	118	14	13	..	..	..	26	2	4	15	3	20
Melanoma	..	..	..	..	..	..	4	2	50	11	3	27
Lymphoma	23	3	13	..	..	..	..	..	..	33	13	38
Leukemia	..	..	..	..	..	..	..	..	..	18	7	41
Myeloma	..	..	..	..	..	..	..	..	..	11	5	45
Total cases	829	..	..	623	..	..	439	..	..	542	..	..

\* Some miscellaneous tumors and all neoplasms of unknown origin have been omitted from the four series. Percentages are given as rounded figures.

*B. Metastasis to Neuraxis Only.*—Local involvement of lymph nodes about the primary site (i. e., involvement of the hilar nodes in the presence of pulmonary tumor) is excluded from this discussion. The neuraxis was the only site of secondary involvement in 9 of the 207 patients (4%). The primary sources of these metastases were as follows: lung 4, breast 2, kidney 2, and thyroid 1. The brain was invaded in eight of these nine patients; the meninges in one. Rupp<sup>9</sup> found the lung to be the commonest source of neoplasms which involved only the cranial cavity. He reported 42 of 150 cases (28%) of metastatic brain tumor with intracerebral metastases alone.

*C. Sites of Metastases in the Neuraxis.*—The meninges alone were implicated in 86 of the 207 patients. The pachymeninges were involved much more frequently than the leptomeninges. There were metastases—to both the meninges and the brain in 36 patients, and the brain alone was the site of metastases in 85 patients.

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Metastatic lesions within the spinal cord were not found in any of the 76 spinal cords examined. The spinal dura alone was implicated in 14 cases; the cranial and spinal dura, in 9, and in 6 instances there were both spinal dural and intracerebral metastases. Some primary tumors tend to metastasize more commonly to the meninges, and others tend to metastasize to the central nervous system. There were 71 patients with primary neoplasms of the breast. The meninges alone were involved in 35, the brain and meninges in 18, and the brain alone in 18. In contrast to this, of the

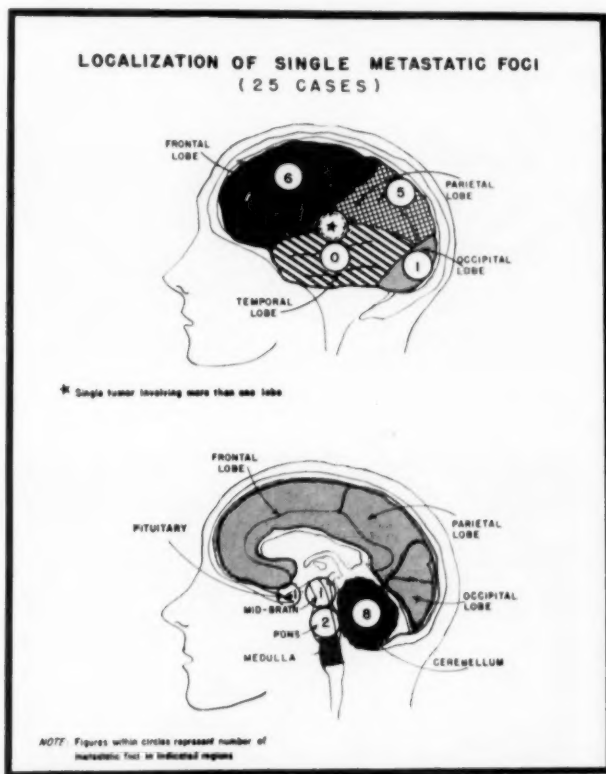


Fig. 3.—Schematic drawing to show the location of single metastatic foci.

50 patients with pulmonary tumors metastases to the meninges alone were found in only 8, 4 to the brain and meninges together and 38 to the brain alone. The tendency to metastasize to meninges occurs also in patients with cancer of the prostate, multiple myeloma, malignant lymphomas, and leukemia. Parenchymal metastases were commoner in cases of pulmonary and renal carcinomas and sarcoma.

A point of major concern from a therapeutic standpoint is whether the metastases are solitary. Operative therapy frequently depends on this. Solitary metastases were found in 20% of 121 patients with parenchymal involvement. The principal sources were as follows: lung, 13; breast, 4, and kidney, 2. There were 12 additional patients with a single central nervous system lesion, but in whom there were also

meningeal metastases. It is believed by some that metastases from the kidney are more likely to produce solitary foci in the nervous system. Willis<sup>6</sup> stated that these occur "perhaps more often than [with] any other tumor." Our data are not in accord with this observation. Of the 10 patients with renal cancer there were 7 cases of intracerebral metastases, and of these only 2 were solitary, which incidence is similar to the average for all tumors in this series. Solitary carcinomatous metastases occurred most frequently with those carcinomas which metastasized most frequently

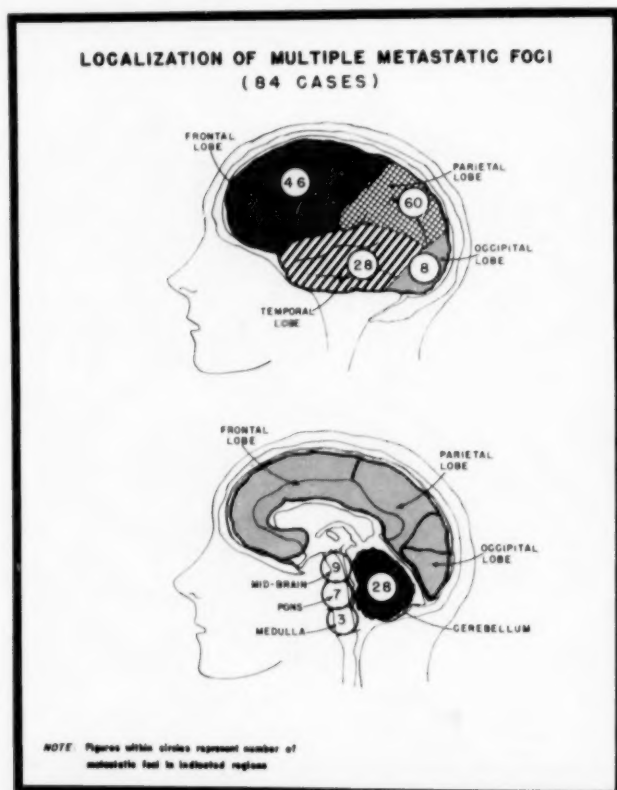


Fig. 4.—Schematic drawing to show the location of multiple metastatic foci.

to the brain. The 25 single metastatic foci were distributed as shown in Figure 3. The cerebellum had more solitary foci than any of the cerebral lobes, but the total number of cases is small. In the 13 patients with cerebral lesions the frontal and parietal lobes were most frequently involved. The distribution of tumors in the 84 brains with multiple lesions is shown in Figure 4. The parietal lobe was the commonest site of metastatic invasion, and the frontal lobe a close second. The basal ganglia were involved in 29 cases.

*D. Macroscopic Appearance of Metastatic Tumors in the Central Nervous System and Meninges.*—Intracerebral metastases are most frequently recognized because

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they are well demarcated from the surrounding neural parenchyma (Fig. 5) and often can easily be shelled out. Rarely the edge may be irregular and thus suggest an infiltrating glioma (Fig. 6). The lesions are more frequently multiple than single. They are usually round or oval in shape and most frequently are gray and granular in appearance. They may affect both gray and white matter but are commoner in

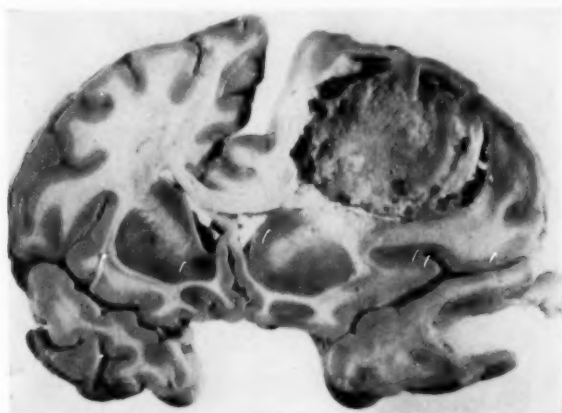


Fig. 5.—Typical appearance of a well-demarcated metastatic neoplasm in a case of bronchogenic carcinoma.

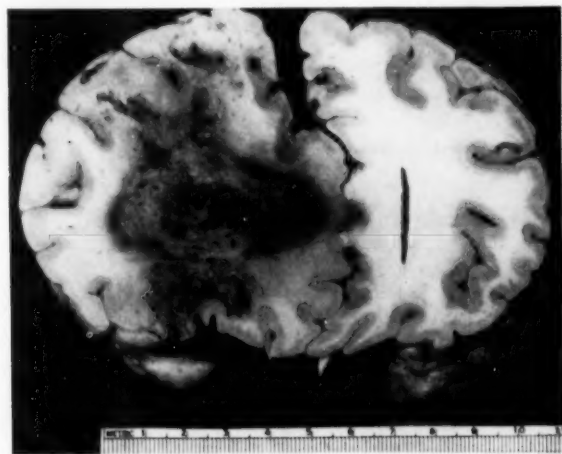


Fig. 6.—A metastatic hypernephroma with irregular edges and grossly resembling glioblastoma multiforme. There is swelling of the involved hemisphere.

white matter because of the greater bulk of this tissue. They frequently occur at the margin between gray and white matter, but this is not always true (Fig. 7). They may be found in gray matter alone, or deep in the white matter. Any part of the cerebrum may be affected, and usually those portions which are greater in volume are more frequently affected.



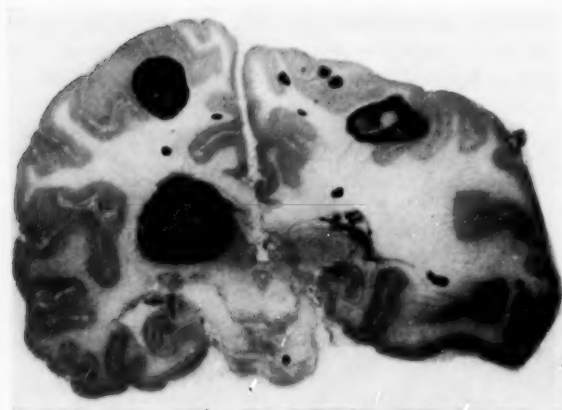


Fig. 7.—Multiple metastases of different sizes seen as dark masses in a Nissl preparation. Metastases occur in gray and in white matter, as well as at the corticomedullary junction.



Fig. 8.—Metastasis of a primary bronchogenic carcinoma to the pons. The central material is semiliquid and necrotic. The appearance mimics that of an abscess.



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The size of metastatic tumors is variable. They may form only barely visible foci, and, indeed, some can only be seen microscopically. They range in size usually up to 6 cm. Larger masses are uncommon. They may be solitary or occur by the dozens.

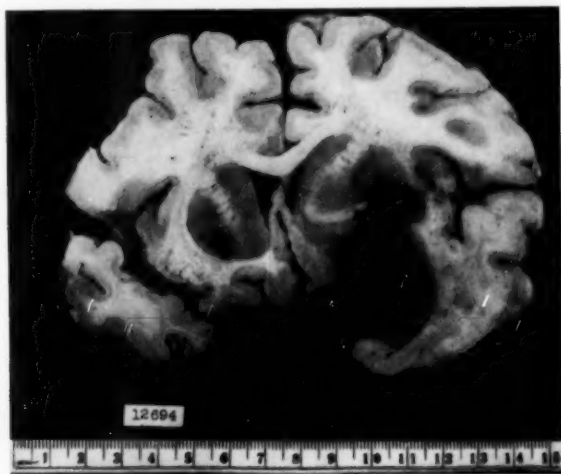


Fig. 9.—A hemorrhagic metastatic hypernephroma in the left temporal lobe near the middle cerebral artery. The sharp line of demarcation suggests an aneurysmal wall with secondary hemorrhage into the putamen.

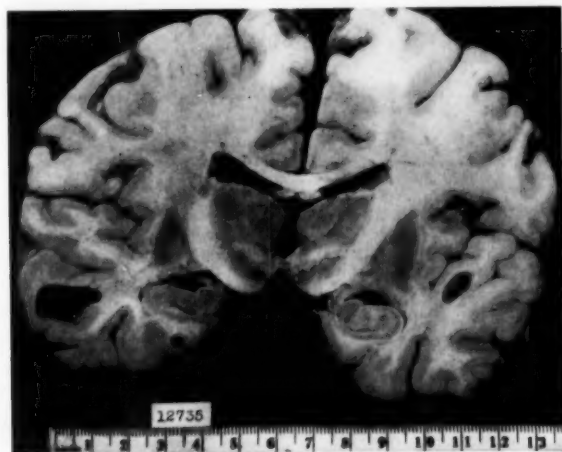


Fig. 10.—Multiple metastases from carcinoma of the bronchus. The tumors in the temporal lobes have clear, yellow centers, and neoplastic tissue is visible only microscopically.

The usual gray, granular appearance in some cases may undergo variations. There may be necrotic foci scattered through the tumor, and, especially in instances of pulmonary carcinoma, the entire center may become necrotic (Fig. 8). Centrally



Fig. 11.—Frontal poles covered by creamy material which has the appearance of leptomeningitis.

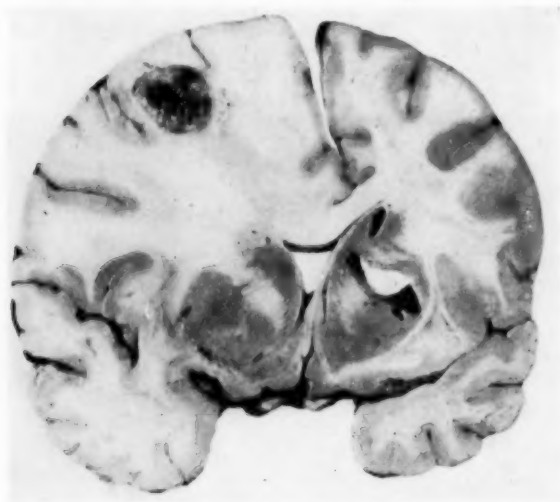


Fig. 12.—An extreme degree of swelling of the left cerebral hemisphere in association with a single metastasis from carcinoma of the thyroid gland. The swelling affects mostly the white matter. As a result, there is marked distortion of the ventricular system and a shift of the midline. The right lateral ventricle is a crescentic slit. The two openings of the right side are artifacts.

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necrotic foci surrounded by granular tissue may thus resemble brain abscesses. This resemblance is important surgically, because the inner necrotic material not only may deceive macroscopically but may appear as an inflammatory process microscopically and thus lead to an erroneous diagnosis of cerebral abscess. It is therefore important for the surgeon and the pathologist to study the nature of the wall surrounding any abscess-like lesion.

In some instances the tumor may be hemorrhagic and mimic the appearance of a thrombosed aneurysm if the lesion lies near a major artery (Fig. 9), or of simple hemorrhage elsewhere in the brain. Less common are metastatic tumors in which the central portion contains clear or cloudy liquid material (Fig. 10). In such instances the tumor may be lined by thin layers of acinar structures, and the neoplas-

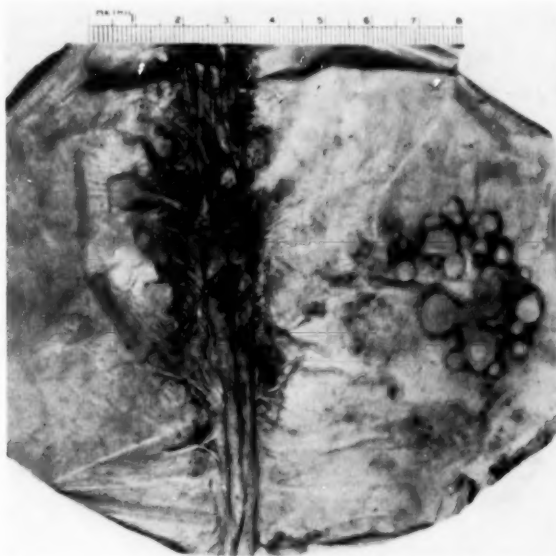


Fig. 13.—Cerebral dural surface containing numerous wart-like excrescences of metastatic tumor in a case of metastatic carcinoma of the breast.

tic tissue may not be macroscopically visible. Others of these tumors have thicker layers of neoplastic tissue, which then appear in the usual gray and granular fashion. In the presence of severe jaundice the neoplasm may be bile-stained. Calcification of metastatic tumors is rare.

There are other uncommon variations in the appearance of these neoplasms. A leptomeningeal carcinomatosis may not be grossly visible, but when it is macroscopically apparent, the meninges are cloudy and the appearance is that of a purulent meningitis (Fig. 11). Capillary tumor emboli may become evident by producing small infarcts, especially of gray matter. It is rare for major vessels to become occluded by such emboli.

The surrounding cerebral tissue may become extremely swollen (Fig. 12). This swelling has no relation to the size, or number of metastases, and its cause is

unknown. A single metastatic nodule may be accompanied by a large amount of swelling; on the other hand, there may be no swelling with numerous lesions in the brain. Pulmonary neoplasms were accompanied by swelling more frequently than any of the other types, and this condition undoubtedly contributed to the rapidity of development of signs in these cases.

In the dura metastatic tumors are also gray and granular. The dural venous sinuses are seldom invaded. The neoplasms may be on either surface of the dura, although the cerebral epidural surface is usually implicated by extension from the cranial bones. The cerebral dura may contain flat plaques, which are single or multiple, small or large (Fig. 13). They tend to be present at sites other than the Pac-



Fig. 14.—Entire surface of the dura covered by a "helmet" of granular metastatic tumor with compression of the underlying cerebral hemispheres.

chionian granulations, as distinguished from meningiomas, but this finding is not invariably true. Indeed, it may be difficult on macroscopic grounds to distinguish between these neoplasms unless the metastatic tumor is necrotic. The dural metastases may become confluent and produce a "helmet" of tumor infiltration (Fig. 14), but this usually spares the dural venous sinuses. When dural metastases result in bleeding, a subdural hematoma may form. Such hematomas do not result in clinical signs.

In the spinal canal metastatic tumors are most frequently epidural in location. They seldom penetrate the inner surface of the dura. Damage to the spinal cord is produced by vertebral infiltration and fracture, by compression of blood vessels, by epidural compression of the spinal cord, or by infiltration of roots (Fig. 15). Intra-

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spinal metastases within the substance of the spinal cord are extraordinarily rare. Leptomeningeal infiltrations in this region may result from downward seeding of neoplasm from above. The appearance is that of a white (or hemorrhagic) cloudy meninx, although, as in the cerebrum, the tumor cells may be recognized only microscopically.

The microscopic appearance of these tumors has been recounted in numerous excellent publications, and we have little to add. More than half of the carcinomas were acinar in character, and about one-third were anaplastic. Only 12% were of the squamous type, the lung being the only common source of these tumors. In 77%



Fig. 15. Spinal dura opened to show the cauda equina. Two lumbar nerve roots lying laterally are swollen by metastatic tumor from carcinoma of the nasopharynx.

of the cases the secondary tumor was similar to the primary neoplasm in degree of differentiation. In about 10% the cerebral tumor was more differentiated, and in a similar number there was less differentiation than in the primary focus.

#### COMMENT

From the preceding data it is apparent that characterization may be made of the picture peculiar to the two commonest types of metastatic tumors. The other groups are small in number and do not justify generalizations concerning their behavior.

Metastases to the brain from carcinoma of the bronchus are among the most malignant. There is usually a short interval of about five months between the onset of the primary disease (if known) and the signs of cerebral involvement. In some

cases the neurologic signs are the first to be noted. Once intracranial signs appear, the course is extremely short, the patients surviving an average of only three months. The absolute number of both primary lesions and metastases is higher in men than in women, but there is a higher proportion of metastases in women. The spread is far more frequent to the central nervous system than to the meninges. The brain may be the only site of metastases in a few cases. This involvement occurs most commonly with pulmonary neoplasms, probably because they are the most frequent invaders of the brain. Metastases to the cerebrum may be solitary, but the course is usually so rapid that this feature is of little avail prognostically. These tumors are frequently accompanied by cerebral swelling.

Carcinoma of the breast with intracranial metastases may present a different picture. Although obviously a malignant neoplasm, nevertheless the interval between the onset of the primary growth and that of the metastases is longer than in the case of the lung and occasionally may be many years. Similarly, the duration of life after the onset of neurologic symptoms is longer than with pulmonary tumors and in a small number of instances is compatible with life for as long as four years. In many instances there may be no signs related to the cerebral metastases, and death results from other causes. The sexual incidence is, of course, dominated by the fact that breast carcinoma is rare in males. The metastases in half the cases are found in the dura alone. This is in part the explanation for the relatively more benign course. In addition, cerebral swelling is less common.

It is interesting that neoplasms of the gastrointestinal tract, including the esophagus, stomach, colon, and rectum, although occurring commonly, have an extremely low incidence of metastases to the neuraxis. Other organs with a low rate of metastasis include the ovaries, pancreas, gall bladder, uterus, cervix, and urinary bladder. It should be noted, however, that any malignant neoplasm is capable of metastasizing to the brain or meninges. The explanation for the low frequency of metastases of some tumors and the high frequency from carcinoma of breast, lung, and kidney is not readily apparent. In the case of the lung, the ability of tumor cells to enter the pulmonary vein and thereafter the left side of the circulation may perhaps explain the behavior of this tumor, but this explanation is hardly feasible for carcinoma of the breast without intrathoracic extension, or for carcinoma of the kidney. The meningeoarachnoid or vertebral system of veins described by Batson<sup>14</sup> is not a wholly acceptable alternative explanation.

The transfer of tumor cells by this route has been considered by Batson, and there is some experimental evidence to show that such a possibility exists.|| But if correct, it is difficult to explain the rarity of metastases within the meninges and substance of the spinal cord. The movement of such tumor emboli against the stream of circulation in the dural sinuses remains to be proved. The rarity of metastases in the dural sinuses and the presence of many metastases deep in the cerebral substance are best explained by arterial blood stream invasion rather than by movement against the flow of cerebrospinal fluid in the perivascular spaces.

The hypothesis of passage of tumor cells through the vertebral veins is aided by failure to find pulmonary metastases in instances of cerebral metastases. In this series there was gross or microscopic evidence of pulmonary involvement in 75%

|| References 15 and 16.

of the cases. The remaining 25% without evidence of pulmonary metastases may be accounted for by at least two other explanations. First, the lung is difficult to study fully, and small metastases easily may be missed. Secondly, emboli may consist of single or few cells and pass the pulmonary filter to lodge in the brain or other organs on the left side of the circulatory system. More definite proof of the role of the vertebral veins in metastasis is needed.

Clinically, most of these patients presented relatively simple neurologic problems because in most instances the existence and site of the primary growth were well recognized. Some points of clinical and theoretical interest arose from a review of the findings. Headaches were commoner with parenchymal than with meningeal lesions. This finding is somewhat unexpected, because it might be argued that pain-sensitive structures are commoner in the meninges and hence pain should be encountered more frequently. In cases of dural and leptomeningeal infiltrations there were rarely clinical evidences of meningeal irritation. Convulsions also were uncommon with meningeal neoplasms, despite the fact that the duration of life was longer in these instances.

Another interesting feature was the absence of extrapyramidal signs, although there was 29 cases with implication of the basal ganglions. In some of these cases there were, in addition, widespread metastases to other regions of the brain, but extrapyramidal signs were still absent. A corollary of this would be that the development of extrapyramidal signs during the illness of a patient with cancer is probably related to another process and not to intracerebral metastasis.

In the sphere of the cranial nerves, papilledema was not common (15% of the cases), and hence its absence does not aid in ruling out metastatic brain disease. Alterations of pupillary reactions to light and on convergence are also rare, except when there is a great increase in intracranial pressure, or terminally. Implication of multiple cranial nerves is rare in true metastases, although commoner in instances of extension of neoplasms at the base of the skull, such as that from tumors of the nasopharynx.

There are some features in this series which are different from those in many reported series of neuraxial metastases. There are more patients with carcinoma of the breast than are usually found. This incidence is related to the large number of such patients who enter the Neoplastic Service. The unusually high percentage of metastases (35%) in relation to the number of brains examined has been mentioned. There are many selective factors which play a role in producing so high a figure. In the first place, Montefiore Hospital is not a general hospital, and it has large neurologic and neoplastic divisions. Few children are admitted, thereby eliminating some of the tumors peculiar to this group. Many of the patients are chronically ill and are frequently in the late stages of their disorders. A series of this type is therefore more likely to represent the final outcome of systemic cancer. Many institutions cannot have direct knowledge of this style because patients with known disseminated cancer are excluded. The complete study of the patient is more likely to occur at this hospital than in one in which the patient is lost after an initial study or attempted surgical removal of the primary tumor. The Home Care program aids in bettering the follow-up studies.

The patients at this hospital with known neoplasms received intensive therapy—surgical, supportive, antibiotic, radiologic, hormonal, and chemical. This factor,



too, might have played a part in determining the extent of metastasis. The necropsy rate and the frequency of examination of the nervous system when necropsy is performed are additional variables. If the brain is not examined routinely, a low estimate of the frequency of metastasis will result. Overestimation may occur if the brain is examined primarily in those patients with cancer who have symptoms of neurologic disorder. In these cases permission for complete necropsy may be specially sought, and more limited study will be accepted in instances where neurologic signs are lacking. Routine examination of the brain will disclose a surprisingly high incidence of neuraxial metastases with death occurring before these become symptomatically apparent (32% in this series).

The multiplicity of variables makes it difficult to decide what the frequency of cerebral metastases would be in a wholly unselected group of cancer patients. It seems probable that it would be higher than the approximate 5% indicated by some studies (Table 1).

## SUMMARY

The clinical and pathologic findings are analyzed in 207 cases of metastatic neoplasms in the central nervous system and meninges. There were neuraxial metastases in 35% of these cases. Reasons for this unusually high percentage are discussed. Data are presented to show the capacity of the various primary growths to metastasize to the nervous system. The contrast between parenchymal and meningeal lesions is stressed and illustrated by significant differences in the biologic behavior of neoplasms arising in lung and in breast.

The different parts of the brain are affected primarily according to their bulk. Solitary metastases are found most frequently with those neoplasms occurring most frequently in the brain, rather than with specific tumor types. Metastasis of tumors is considered most likely to be by way of the arterial blood supply. Some of the numerous variant appearances of metastatic tumors are illustrated.

In this necropsy series about one-third of the metastases were asymptomatic. When symptoms occurred, the commonest were motor signs, mental and personality changes, and headache. Surprisingly, the last symptom was commoner with intracerebral lesions than with meningeal involvement. Extrapyramidal signs did not occur in these cases of cerebral metastases, even though the basal ganglia frequently were invaded.

Mr. Antol Herskovitz supplied most of the photographs.

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## SERUM LIPID STUDIES IN MULTIPLE SCLEROSIS

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LIPID STUDIES in multiple sclerosis should have a special significance because the disease process involves a breakdown of the lipid-rich myelin. Studies on the serum lipids in this disease have been reported recently. Jones and associates<sup>1</sup> found an elevation of cholesterol; Wilnot and Swank,<sup>2</sup> however, examined the total lipid and cholesterol content and concluded that there were no significant changes. Chiavacci and Sperry<sup>3</sup> likewise were unable to find an increase in serum cholesterol, although 11 out of 52 patients did give increased values. Dobin and Switzer<sup>4</sup> found that the free and esterified cholesterol levels are elevated in multiple sclerosis. Schild and associates<sup>5</sup> and Geinitz and associates<sup>6</sup> stated that there was probably an increase in lipoproteins, since the thymol turbidity test, which is frequently positive in multiple sclerosis, depends mainly on the lipids bound to beta globulin. Aird and co-workers<sup>7</sup> carried out ultracentrifuge studies on the sera of 27 patients and found that one fraction,  $S_r$  (12-20), of the lipoproteins was slightly elevated but considered the results merely to be suggestive.

The technique of paper electrophoresis has been used in this laboratory for the determination of serum and cerebrospinal fluid proteins.\* With some variations, this same method can be used for the determination of lipoproteins. Swahn<sup>10</sup> has employed this method for the determination of the distribution of serum lipids and has also proposed a procedure for total lipid estimation. This paper describes the application of these methods to a study of the serum lipid in multiple sclerosis.

### EXPERIMENTAL STUDY

*Quantitative Determination of Total Lipids.*—In the procedure of Swahn<sup>10</sup> blood serum is absorbed on filter paper and stained with Sudan black. Excess dye is removed, and then the stained lipids are extracted and determined colorimetrically. The dye-binding capacity of the serum lipids is directly proportional to their concentration. We have modified the method by determining the concentration directly on the filter paper, using a photoelectric densitometer.

The sera are applied in duplicate to a strip of filter paper in a series of spots by the use of precision micropipettes. From 0.01 to 0.025 ml. of serum can be used; however, 0.025 ml.

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\* References 8 and 9.

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was found to be the most satisfactory volume. The spots are dried in a stream of warm air and the lipids dyed by immersing the strip for three hours in Sudan black solution.<sup>†</sup> The paper is removed; excess dye is allowed to drain, and the paper is washed in three successive baths of 55% ethanol, allowing 15 minutes for each. The bath is occasionally rocked gently for more efficient rinsing. When a number of strips are being treated simultaneously, they are laid side by side in the bath and not permitted to overlap. The paper is then air-dried; the lipid spots appear blue-black on a pale gray background. The densities of the dyed spots are measured with a Photovolt densitometer.<sup>‡</sup> From the readings, a curve is constructed which gives the optical density of the dyed spot as a function of the area under the curve. The area is converted into a total lipid value by reference to an olive oil calibration curve.

The calibration is based on the assumption that olive oil absorbs the dye on the paper in proportion to its concentration, as do the lipids of the blood serum. Swahn<sup>10</sup> found that the uptake of the dye is independent of the chemical nature of the lipid, since triolein, corn oil, and

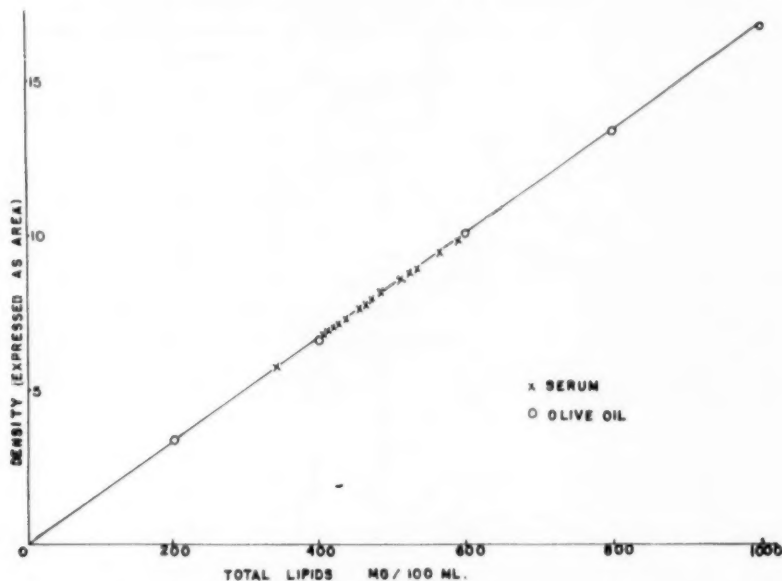


Chart 1.—Standardization curve for the estimation of total lipids.

lecithin all fall on the same straight line as the lipids of the blood and similarly follow Beer's Law. By the use of micropipettes, triplicate spots of a 1% alcoholic solution of olive oil are applied to the paper. The quantities of olive oil used are appropriate to the range of lipid values found in blood sera. The staining and measurement of the spots are carried out by the method previously described. The lipid contents of the oil spots are then plotted against the areas of the densitometer curves (Chart 1). A straight line is obtained within the range of 0 to 1,000 mg. of lipid per 100 ml. of solution. If the density of such an area obtained from a serum spot is measured, its total lipid content can be read directly from the chart. As a control, gravimetric

<sup>†</sup> Sudan black solution is prepared by adding 1 liter of 60% ethanol to 1 gm. of Sudan black and heating to the boiling point. After cooling, the solution is filtered to remove suspended particles of the dye. Owing to evaporation, Swahn stated that the final solution contains 50-55% ethanol.

<sup>‡</sup> Model 525, manufactured by The Photovolt Corporation, 95 Madison Ave., New York.

determinations were made on serum samples by the method of Wilson and Hanner,<sup>11</sup> the results obtained being in excellent agreement with those given by the direct photometric method. The method was compared by Swahn<sup>10</sup> with other standard total lipid methods on a large number of normal and pathological blood sera, and good agreement was found. While free cholesterol gives no color, this fact apparently does not reduce the accuracy of the method, probably because of the relatively low concentration of free cholesterol in serum.

**Electrophoresis of Lipoproteins.**—The lipids in the serum are not present in free form but, rather, occur in combination with proteins. Because of this union, the lipids will move in an electric field and can be determined by zone electrophoresis.

For the electrophoretic distribution studies two types of apparatus have been used, with similar results. The first is that of Durrum,<sup>12</sup> in which the paper strips are suspended centrally from a rack with the ends immersed in buffer-containing troughs bearing the electrodes. The second is the Electrophorograph,<sup>§</sup> in which the paper strips are supported horizontally. The paper

*Distribution of Lipoproteins in Sera from Normal and Multiple Sclerosis Cases*

Case No.	Total Lipid. Mg. per 100 Ml.	Lipoproteins, %		
		Alpha-1	Beta	Gamma Region
		Normal		
1 .....	...	18	59	23
2 .....	...	27	51	22
3 .....	450	10	54	36
5 .....	425	14	61	25
6 .....	565	15	74	11
8 .....	490	14	67	19
13 .....	440	26	57	17
32 .....	410	14	70	16
Pool .....	465	19	61	20
Average .....	463 ± 57	17.7 ± 5.6	61.6 ± 7.4	21.3 ± 5.9
Multiple Sclerosis				
259 .....	590	17	60	23
265 .....	425	33	49	18
268 .....	485	32	56	12
269 .....	530	19	68	13
271 .....	455	24	42	36
280 .....	340	14	86	0
301 .....	525	15	43	42
304 .....	410	23	65	12
308 .....	405	25	52	23
312 .....	420	21	64	15
318 .....	475	14	71	15
322 .....	592	20	60	20
Average .....	471 ± 67	21.4 ± 6.4	59.7 ± 12.6	18.9 ± 9.6

strips are immersed in the buffer and blotted on a sheet of filter paper before the sample is introduced. Approximately 0.02 to 0.03 ml. of serum is applied to the paper with a micropipette for the lipid determination, and at the same time 0.01 ml. of the serum is applied to another strip for measurement of the proteins; the latter strip serves as a position marker for the lipoproteins.

Barbital buffer (pH 8.6, ionic strength 0.1)<sup>12</sup> and a current of 240 volts are used. Separations were run for three, four, and six hours, and it was found that the four-hour period gave the clearest picture of the lipids, with distinct measurable peaks. The paper strips are dried at 100 C. for 10 minutes to immobilize the proteins on the paper. The protein-marking strips are dyed with bromophenol blue, as previously reported,<sup>8</sup> and the lipids with Sudan black, as described for the quantitative lipid determination. In our hands the results with Sudan black were superior to those with oil red O<sup>13</sup> and with osmic acid.<sup>14</sup> The lipoproteins appear to be separated into several dark-colored bands and are evaluated with the densitometer. Super-

§ Made by Gerard Pleuger, S. A., 227 Avenue d'Amerique, Antwerp, Belgium; Distributor in United States, C. A. Brinkmann and Co., Great Neck, Long Island, N. Y.

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imposition of the density diagrams of the two strips will relate the positions of the lipoproteins to the proteins. Perpendiculars are dropped from the minima of the curves to the base line, and the relative areas between the perpendiculars, measured with a planimeter, are expressed as percents of alpha, beta, and gamma lipoproteins.

**Results and Comment.**—Sera from 12 established multiple sclerosis cases are compared with sera from 8 normal persons and with a pooled sample of 4 normal sera. The values, together with their averages and standard deviations, are given in the Table. The total lipid values for the normal sera vary from 425 to 565 mg. per 100 ml. serum, with an average value of 463 mg. per 100 ml., and for the multiple sclerosis patients, from 340 to 592 mg. per 100 ml. of serum, with an average value of 471 mg. per 100 ml. Wilmot and Swank<sup>2</sup> obtained values in the range of 477 to 722 mg. per 100 ml. for the normal and 486 to 767 mg. per 100 ml. for multiple

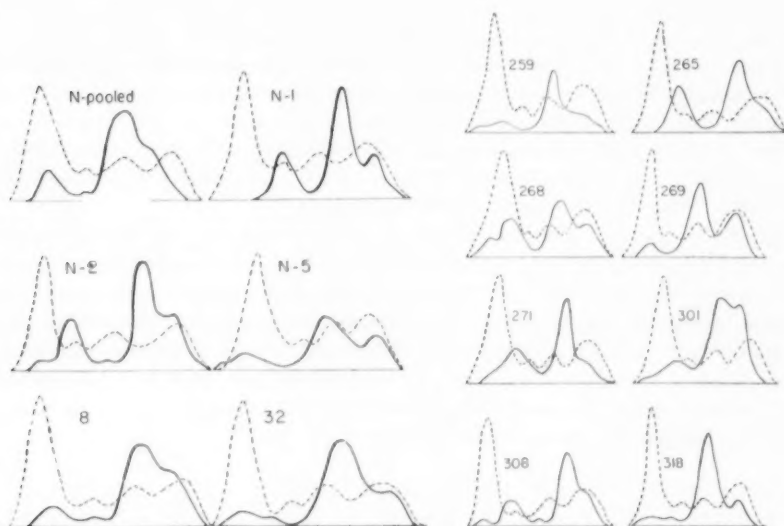


Chart 2 (left).—Distribution patterns of lipoproteins (solid lines) and proteins (dotted lines) in typical normal sera.

Chart 3 (right).—Distribution patterns of lipoproteins (solid lines) and proteins (dotted lines) in multiple sclerosis sera.

sclerosis patients; they conclude that the average values of 591 mg. per 100 ml. for the normal persons and 639 mg. per 100 ml. for the multiple sclerosis patients do not represent significant differences. Our data confirm these findings.

In every case the beta lipoprotein was the major component of the electrophoretic pattern of the lipoproteins, comprising about 60% of the total lipids. In the normal sera, the neutral fats, which remain near the starting point of the electrophoresis on the strip, and which are here designated as gamma lipoproteins, are present in about the same concentration as the alpha-1 lipoprotein. In the multiple sclerosis sera there is a trend toward an increase in the alpha-1 fraction, with a corresponding decrease in the lipids in the gamma region. In one case, Case 280, in which the total lipid content was extremely low no lipid could be detected in the gamma region.

When a series of six determinations were made upon the same sample of normal serum, the average values and standard deviations for the alpha-1, beta and gamma lipoproteins, respectively, were  $18.2 \pm 2.8$ ,  $52.4 \pm 3.8$ , and  $30.0 \pm 3.0$  mg. per cent. As would be expected, the standard deviations of the averages obtained upon both the normal and the multiple sclerosis subjects, as shown in the Table, are greater than those obtained on the replicates of the same serum. However, in the normals, the differences in standard deviations are not large, indicating a general uniformity of lipoprotein pattern in the normal sera. For all three fractions in the multiple sclerosis sera the standard deviations are greater than those in the normal, and markedly so for the beta and gamma lipoproteins. It is evident, therefore, that there is greater variability in the lipoproteins in these cases, but only a much larger series of determinations will reveal whether the variability is significant.

A number of typical distribution patterns of both normal and multiple sclerosis sera are given in Charts 2 and 3. The proteins (dotted lines) are included so that the relationship of the lipoproteins to them may be observed. When the electrophoresis is run for only four hours, the best time for the lipoprotein separation, the other proteins do not separate so sharply, particularly in the alpha region. It will be noted that the lipid peaks do not coincide exactly with the protein peaks; the alpha-1 lipoprotein moves ahead of the alpha-1 protein and is close to the albumin. Kunkel and Slater,<sup>10</sup> using phosphate buffer pH 6.5, obtained a pattern in which the alpha-1 lipoprotein moved ahead of the albumin.

If, during the demyelination process in multiple sclerosis, lipid is released into the blood stream uncombined with protein, it should act as neutral fat and should not move during electrophoresis. This condition should lead to an increase in the gamma lipoprotein fraction. No such increase was observed. That abnormalities of the lipids in the tissues do not necessarily extend to the blood was observed in other diseases. In grave disturbances of lipid metabolism, such as Niemann-Pick or Tay-Sachs disease, where lipids accumulate in various organs and in the neuron cells, no changes were found in blood lipids.<sup>16</sup>

#### SUMMARY

The lipid content of normal and multiple sclerosis sera was measured by staining the lipids absorbed on filter paper strips and determining quantitatively the density of the stained area with a densitometer. The results were in good agreement with those obtained by other methods. There was no significant difference between the total lipid content of the normal sera and that of multiple sclerosis sera.

The distribution of the lipoproteins in both normal and multiple sclerosis sera was determined by the method of paper electrophoresis. While greater variability was observed in the patterns in multiple sclerosis, the 12 cases in which electrophoreses were run were not sufficient to permit significance to be assigned to these variations.

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## BIOLOGICAL SIGNIFICANCE OF HEAD POSTURE IN UNILATERAL DISEQUILIBRIUM

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UNTIL now the significance of head posture has been considered chiefly from the symptomatological point of view. It is common knowledge that changes of head posture occur in general disturbances, such as meningeal or muscular disorders, or as a corrective posture in local lesions producing such disturbances as diplopia, homonymous hemianopsia, or unilateral positional vertigo. Deviation of the head occurs also in posterior fossa tumors and for some time may be the only sign present.

The classic investigations of Magnus<sup>1</sup> showed that head posture not only undergoes passive alterations but can, under certain circumstances, effect an active influence. He revealed in his experiments on animals that turning of the head to one side caused extension of the "facial" limbs and flexion of the "occipital" limbs. Tonic neck reflexes were later observed, as is well known, under pathological conditions in human beings too. They appear with certain variations, particularly in diffuse cerebral disorders of traumatic or inflammatory origin, as well as in tumors of the brain, in children and in adults alike.

The discovery of the tonic neck reflexes disclosed, first, the existence of an extended motor relationship among the separate members of the body. It revealed further the important fact that head posture influences the tone and position of the extremities, as is apparent under pathological conditions, but is certainly effective under normal conditions too.

After the general acceptance of these conclusions further scientific interest in the significance of head posture seemed to have exhausted itself for several decades. The interesting investigations which Goldstein\* carried out later on the tendency to optimal behavior, wherein the problem of head posture is dealt with too, seem not to have received adequate consideration. Clinical experiences gained recently from further observations may, however, show very well the significance of head posture from the biological point of view. These experiences concerned especially patients with systematized unilateral disturbances of equilibrium.

### I. POSTURE OF THE HEAD IN UNILATERAL DISEQUILIBRIUM

The posture of the head in unilateral disequilibrium assumes a special interest. In some patients with this condition the spontaneous posture of the head does not alter visibly. In those patients, however, in whom unilateral disequilibrium consti-

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\* References 2 and 3.



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tutes the basis of the sensorimotor induction syndrome a deviation of head posture occurs almost constantly. This spontaneous change represents in these cases a partial manifestation of the existing unilateral displacement of the body and its homolateral extremities. These patients keep their head inclined to one side mostly, without being aware of it. The abnormal position of the head appears in some cases only after closure of the eyes, but where a spontaneous change of head posture already exists, it is then increased. The direction of the deviation corresponds as a rule with the side of the disequilibrium, and only in fewer, severer cases with the opposite side. Sometimes a change of head posture from the homolateral to the contralateral side occurs during the course of the disease. The newly acquired position of the head in these patients is characterized by its conformity and constancy. Thus, when the patient, with his eyes closed, has his head turned to the extreme right or left and is asked to return it to the midline, he invariably brings it back to the previously held abnormal spontaneous position, either passing or not reaching the midline, according to the direction of turning. In some of these patients even an automatic movement of the head may occasionally occur, without their being aware of it. The head, passively turned to the contralateral side, returns then in a series of jerking movements to the abnormal spontaneous position.

### II. INFLUENCE OF HEAD POSTURE ON VARIOUS FUNCTIONS

Of the various functions which the position of the head influences, the body posture will be dealt with first. The following observations on two patients with a tendency to fall to one side may serve as illustrations.

CASE 1.—J. B., a man aged 41, had been suffering from attacks of dizziness for two years, since, as he said, he received a blow on the back of the head. He felt as though he was turning around, while his surroundings did not move. The attacks were sometimes associated with nausea and vomiting, and from time to time he also saw double.

Neurological examination disclosed the following abnormal signs: The left pupil was larger than the right and did not react to light. Nystagmoid movements were present on fixation to either side. Paralysis of the left inferior oblique muscle was found on the right side, with slight adiadochokinesis of the right arm. The abdominal reflexes were present, but the knee and ankle reflexes were absent. The Babinski sign was elicited on both sides. Electroencephalographic, pneumoencephalographic, spinal fluid, and internal examinations were all normal.

This patient, with the diffuse clinical picture, which was assumed finally to be that of disseminated sclerosis, showed in addition a right-sided disturbance of equilibrium which manifested itself in an abnormal body posture and gait. When walking forward with his eyes closed, he deviated to the right; when walking backwards, to the left, and when this was repeated several times, the *marche d'etoile* resulted. With regard to body posture, the patient showed a slight tendency to fall to the right even when his eyes were open, and when his eyes were closed, this tendency was noticeably increased (Fig. 1). This tendency to fall to the right was influenced by the change of head posture in the following way: When the patient's head was turned or inclined passively to the left, the tendency to fall to the right increased, but when it was turned to the right, this tendency was subjectively and objectively removed (Fig. 2). This result was regularly obtained on repeated examination.

The increased tendency to fall to one side when the head was turned to the left calls to mind the mechanism of nystagmus provoked by only a certain position of the head. The increased or abolished tendency to fall produced by changing the

position of the head corresponds to the features of the Magnus neck reflex as applied to the function of equilibrium. The potential ability of the organism to correct the tendency to fall by an adequate change in head position was demonstrated in this patient, whose spontaneous head posture was normal. As will be shown later, the organism is able to exploit this potential corrective ability in the presence of unilateral disequilibrium by developing special symptomatological features.

CASE 2.—B. K., a woman aged 45, underwent cholecystectomy eight years previously. Since that time she had not suffered from any visceral complaint. Fourteen years prior to consultation she had an attack of rotatory vertigo for the first time, accompanied by nausea and vomiting. At about the same time she began to suffer from a slight ringing in the right ear, and the hearing in the same ear began to deteriorate. Since then she had felt dizzy when moving her head in any direction, but especially upward. She always lay on her right side, since she realized that lying on her left side made her feel that the left side of the room was descending and its right side rising.

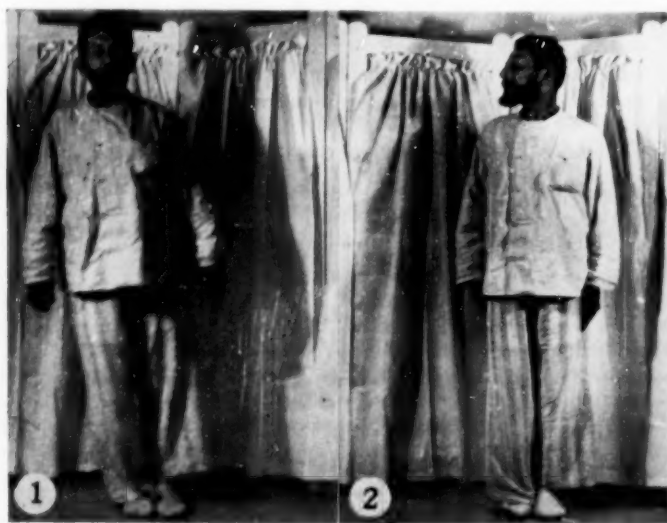


Figure 1 (Case 1)

Figure 2 (Case 1)

For the last five years she had noticed that her head had been making involuntary movements directed toward the right. These movements were aggravated by excitement and were less obvious when she was quiet and relaxed. She noticed also that when touching her left cheek with her left hand, the movements became less frequent.

Clinical examination showed spastic turning of the head to the right. The cranial nerves, optic fundi, pyramidal motility, sensation, and reflexes were normal. The x-ray of the skull and the electroencephalogram were also normal. Otological examination showed signs of old chronic otitis media in the right ear, with a corresponding diminution of hearing of air conduction type. Vestibular caloric tests were normal on both sides.

The patient showed the typical picture of spastic torticollis, illustrating the characteristic influence of emotional factors and *gestes antagonistes*. Further examination revealed that this spastic turning of the head to the right was closely connected with the function of equilibrium. With regard to body posture, the patient showed no departure from the normal apart from spastic turning of the head to the

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right. However, when she was asked to keep her head straight, a distinct tendency to fall to the left was noticed, both subjectively and objectively. This tendency to fall could be abolished at once by returning the head to its usual position. This finding corresponds with the torticollis labyrinthicus described by Curschmann<sup>4</sup> in 1907. He did not recognize, however, the inherent biological mechanism involved. My patient showed, in addition, the automatic head movements described above. When her head, with eyes closed, was turned to the left passively, it nodded back and forth, but mainly to the right, until it returned to its spontaneously held position (Fig. 3). Goldstein<sup>2</sup> made a similar observation in a case of disturbed equilibrium caused by a lesion of the left frontal region of the brain, and Halpern<sup>5</sup> later described another case of left-sided disequilibrium caused by a lesion of the right frontal area of the brain. As was shown in the last two cases and in the one described



Figure 3 (Case 2)

above, the constant aim of the head to return to its spontaneous position reveals the importance of this action for the correction of the static equilibrium. As to my patient, who was possibly predisposed, the correction developing in the course of time assumed the form of a spastic torticollis.

In both patients described above, in the second of whom the impairment was of labyrinthine origin, the disturbance affected solely body posture. But more interesting still in this connection are those patients with unilateral disequilibrium who present the syndrome of sensorimotor induction.<sup>†</sup> These patients show a unilateral motor displacement of the body and its homolateral extremities and various disturbances of sensory perception as well. These latter disturbances are induced by the primary disturbances of the disequilibrium and manifest themselves homolaterally. Under these pathological conditions, which are assumed to originate in the central areas of regulation of the equilibrium, head posture undergoes a more or

<sup>†</sup> References 6 through 10.

less visible alteration and is an almost constant feature of the syndrome. As will be shown in the following case, the change of head posture can influence motor and sensory disturbances as well.

CASE 3.—W. F., a woman aged 35, had suffered from transitory ataxia since the age of 15. It manifested itself by deviation to the right when walking. The patient was examined repeatedly, and two lumbar punctures, performed during this time, were negative. For some months before admission the patient suffered from occasional attacks of dizziness, blurred vision, and unsteadiness of gait.

On admission a systematized right-sided disturbance of equilibrium was found, which had the classic features of the syndrome of sensorimotor induction.<sup>6</sup>

Pathological features, in the motor sphere, were a spontaneous deviation of the head to the right, deviation and descent of the right arm and leg, a tendency to fall to the right, and deviation to the right when walking. In addition, there existed an induced homolateral sensory deviation of the vertical and the horizontal in visual, tactile, and haptic spheres. Apart from these primary sensorimotor phenomena of deviation, secondary disturbances of sensory perception were found too. They manifested themselves in this case in an underrating by the right hand of weight, size, and distance.

With regard to the problem which interests us here especially, it must be stressed that the patient's head was inclined spontaneously to the right, corresponding to the direction of the general tendency of deviation, without the patient being aware of it. The patient's head could be moved freely, actively and passively. When she was asked to place her head in the midline, with her eyes shut, after it had been inclined by the examiner to the right or left, it always returned to its spontaneous position. She stated that she felt better when her head was inclined to the left, while extreme inclination to the right made her feel uncomfortable. Tests revealed that the subjective sensation of the patient had a real somatic basis.

It became apparent that the additional change of head posture, depending on the direction of the alteration, influenced the existing disturbances according to a certain law. Inclination of the head to the extreme left resulted in an improvement of the disturbances, while inclination to the extreme right increased them. When the patient's head was inclined to the left, the spontaneous deviation of the right arm and leg was completely abolished, and the degree of the sensory deviation in visual and haptic spheres was diminished considerably. The same effect was also obtained with regard to the underrating of weight, size, and distance. When the head was inclined to the left, this underestimation disappeared. Extreme inclination of the head to the right, however, produced a systematized deterioration of the various disturbances. The spontaneous deviation of the right-sided extremities was intensified and accelerated; the degree of visual and haptic deviation increased markedly, and the degree of underevaluation by the right hand of weight, size, and distance was also increased measurably. These findings were obtained constantly on repeated examination. The systematic influence of head posture on the various functions, described above, was also observed in similar cases. The following observation may serve as a contribution, showing especially the influence of head posture on sensory function.

CASE 4.—D. A., a woman aged 45, had suffered for the past two years from frequent attacks of dizziness. Six months prior to consultation she noticed unsteadiness when walking. Lately left-sided exophthalmos had been noticed. The basic metabolism rate was +12%. A x-ray of the skull and the pneumoencephalogram were normal.

A mainly left-sided disequilibrium was found in this patient, presenting the symptomatological manifestations of the syndrome of sensorimotor induction.<sup>9</sup>

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Of pathological symptoms, there existed spontaneous deviation of the head to the right, descent of the left arm and leg, past-pointing with the left arm to the right, and tendency to fall to the right. In addition, in the sensory sphere deviation of the visual vertical, on her seeing with the left eye only, a deviation to the left in the haptic sphere, macropsia in the left eye, and macrostereognosis in the left hand were found.

This patient, with the left-sided disequilibrium and the induced sensorimotor manifestations on the left, held her head inclined to the normal right side, in contrast to the patient described above. Here, because of the severity of the impairment, a corrective deviation of the head to the contralateral side took place. This patient, too, was not aware of the spontaneous deviation of her head, which amounted to 10 to 12 degrees on repeated examination. The patient's head could be moved freely, actively and passively, in every direction. When her head was turned passively to the left, the patient stated that this position was disagreeable to her, and that she felt more uncomfortable. When her head was turned passively to the right, she felt relatively at her best. When she was asked, with her eyes shut, to place her head in the midline, after it had been bent passively first to the right and then to the left, it always returned spontaneously to the right.

The effect of head posture on visual functions was seen particularly well in this case. The patient complained of considerable difficulties in reading during the last few months. Sometimes she succeeded in reading small print without effort, while at other times she was unable to read even large print. The letters blended into one another and gave the impression of being superimposed one upon the other. Sometimes, even if the print was relatively small, a letter, a word, or a whole line stood out markedly, as if it were printed in another type. She stated also that she had become doubtful of late as to colors. Her children reminded her, too, that she used the wrong colors when mending clothes, and she noticed herself that she had difficulty in distinguishing white and pink.

These complaints of disturbed vision in patients with unilateral disequilibrium are very characteristic and are the result of the discrepancy between the function of the two eyes in binocular vision. In these patients the eye corresponding with the side of the disequilibrium underwent indirectly typical, induced alterations of visual perception, while being absolutely normal organically. These disturbances were then tested with regard to the influence of head posture upon them. It was shown in this patient, whose left eye was affected, that visual function was improved when her head was inclined to the right and that it deteriorated when the head was inclined to the left. Thus, it could be stated that the deviation of the visual vertical, when she was seeing with her left eye, disappeared when her head was inclined to the extreme right, while it increased on inclination to the left. Further ophthalmological examination with Landau<sup>11</sup> revealed also that acuity of vision and color perception were influenced by head posture. On the basis of repeated comparative testing of acuity of vision on spontaneous inclination of the head to the right, on extreme inclination to the right, and on extreme inclination to the left, it could be shown that it was improved on extreme inclination to the right, while it became worse on extreme inclination to the left. Similar findings were recorded in 1933 by Goldstein and Jablonski<sup>12</sup> in a patient with a left-sided disturbance of equilibrium in whom, as in my patient, inclination of the head to the left caused deterioration; inclination to the right, however, caused improvement of the visual function. Apart from acuity of vision, the influence of change of head posture on color perception was also noticed

in this patient. On inclination of the head to the right differentiation of colors was improved, while it deteriorated on inclination to the left. The impaired color perception caused by this position affected chiefly the various shades of blue, which seemed to be completely black, while recognition of red was undisturbed in every position of the head. The resistance of red to the general dissolution of color perception noted in this case corresponds with the findings in an earlier similar observation of mine, in which the patient at the height of the disease was able to discern only black, white, and red. When the patient of Goldstein and Jablonski saw red, it seemed to extend to all sides, extinguishing all other colors. The exceptional position of red must be recalled here, in view of its favored hallucinatory appearance in the epileptic syndrome. The peculiar position of red noted in this case is of special interest, as it is fundamentally contrary to the position of red in color dissolution caused by an anatomical lesion of the optic nerve, in which it disappears first, while it is always preserved in the indirectly induced color dissolution described here.

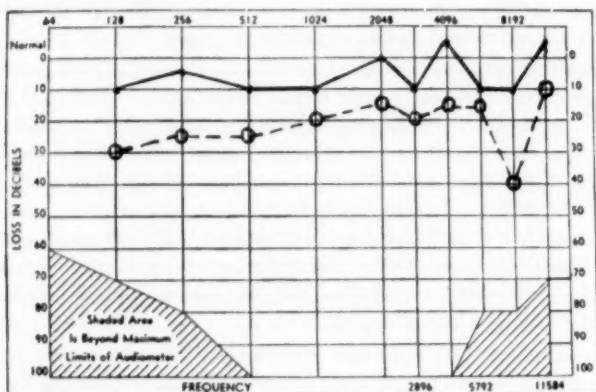


Fig. 4.—Acoustic perception. Solid line indicates perception on spontaneous inclination of the head; broken line, perception on inclination to the extreme right.

As in all similar patients, impairment of acoustic perception was not complained of spontaneously here. Nevertheless, to investigate the influence of head posture on acoustic perception various comparative audiometric tests were performed.<sup>13</sup> On spontaneous inclination of the patient's head to the right the audiometric results were within normal limits. On inclination to the extreme right no marked audiometric changes were obtained. However, on inclination to the extreme left a marked influence on acoustic perception was found in the left ear. All frequencies were affected, and the difference averaged 10 to 20 db., while the range was 5 to 30 db. (Fig. 4). Acoustic perception in the right ear showed no alteration on extreme inclination to the left. Not only visual function deteriorated in this patient on inclination to the left, but acoustic perception as well.

### III. CONCLUSIONS

All observations described above reveal the significance of head posture for the regulation of unilaterally disturbed equilibrium. The clinical picture of the first patient, whose head posture showed no spontaneous deviation, revealed the inherent



## HEAD POSTURE IN UNILATERAL DISEQUILIBRIUM

potential corrective faculty of changed head posture on the tendency to fall. The second patient showed how the organism is able to exploit this possibility in order to exclude the disturbance, although by the pathological means of torticollis. In both patients alteration of head posture effected stabilization of body posture by abolishing the unilateral tendency to fall. The last two patients, with spontaneous inclination of the head, are of special interest in that they show unilateral disequilibrium, representing the syndrome of sensorimotor induction. These patients revealed further that each additional deviation of head posture influenced the motor and sensory functions as well and that, depending on the direction of deviation, a visible impairment or deterioration of functions resulted. The effect obtained by alteration of head posture affected systematically the primary sensorimotor phenomena of deviation and the secondary disturbances of sensory perception. With respect to the gradation and degree of the influence on the various functions, it seems that head posture influences most frequently and powerfully the motor posture of the body and its extremities. Then follow gradually the various disturbances of visual perception, stereognostic perception of size, and, last, acoustic perception which by comparison is relatively the least frequently influenced by changed head posture. In contrast to complaints of impairment of visual function, these patients do not complain spontaneously of impairment of acoustic perception.

The effect produced by changed head posture operates by means of the neurophysiological mechanism of the Magnus neck reflex. In his classic experiments on animals Magnus was able to show only the visible motor effect resulting from changed head posture. The investigations on men reveal further that changed head posture can influence not only motor function but also sensory perception. The Magnus neck reflex in human pathology was, as is well known, observed solely as an interesting phenomenon in severe cerebral degenerative processes. The investigations described above show, moreover, that the neck reflex appears also in the neurodynamics of unilateral disturbed equilibrium as a regulative factor, in that it enters automatically in disturbances of this kind by spontaneous deviation of the head. In the light of the findings of the effect of improvement and deterioration due to the spontaneous extreme inclination of the head to the right or left, the biological significance of this reflex deviation is clarified too. The newly acquired mean position of the head is of importance to the patient in that it renders to the organism its optimal efficiency under the two prevailing contrary extreme tendencies.

### SUMMARY

By means of adequate observations the significance of head posture for the correction of unilateral disequilibrium has been demonstrated. Intentional change of head posture, depending on the direction of deviation, has a systematic effect of improvement or deterioration on the various functions of patients in whom the unilateral disequilibrium has the features of the sensorimotor induction syndrome. These effects produced in man are based on the neurophysiological mechanism of the Magnus neck reflex and confirm, therefore, that this reflex not only influences motor responses, as Magnus demonstrated in his classic investigations on animals, but affects systematically the sensory functions as well. The spontaneous deviation of the head seen in these patients is effected by way of an automatic insertion of a neck reflex and aims at creating a mean position in which the organism attains its optimal efficiency.



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## RAPID DETERMINATION OF OPTIMUM MEDICATION IN RECALCITRANT CASES OF EPILEPSY

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SINCE THE development of the conception of specific anticonvulsant drugs and of methods of testing anticonvulsant activity in animals<sup>1</sup> a long list of new medicines has been introduced into clinical practice for the control of epilepsy. It includes diphenylhydantoin U. S. P. (phenytoin, Dilantin), methylphenylethylhydantoin (Mesantoin), phenacemide (Phenurone), trimethadione U. S. P. (Tridione), paramethadione (Paradione), phethenylate (Thiantoin), and glutamic acid. Others not yet on the market are under investigation, and of course phenobarbital is still a strong contender. Almost alone among recent authors, Arieff<sup>2</sup> maintains 12% of his patients on bromides, and 73% are seizure-free. Even the ketogenic diet is still used,<sup>3</sup> and interest in the use of surgical measures has widened.<sup>4</sup>

The practitioner, and even the specialist, is apt to find himself confused by this plethora, and reference to the literature is not particularly helpful. Usually an investigator who wishes to try a new drug uses it on patients who have been inadequately treated, or not at all. Proceeding on this basis, Locock was able to help 13 out of 14 patients by administration of bromides,<sup>5</sup> and Pollock<sup>6</sup> reports similar results. Lennox reports 65% improvement with phenobarbital,<sup>7</sup> and Merritt and Putnam report 80% of cases unrelieved by phenobarbital to be seizure-free on diphenylhydantoin.\* Kozol reports 90% improvement with Mesantoin<sup>10</sup>; Lennox,<sup>11</sup> 80% improvement in cases of petit mal with trimethadione; Keith, 35.3% with the ketogenic diet<sup>3</sup>; Penfield and Steelman, 55.8% following excision of cortical scars,<sup>12</sup> etc. Many of these reports may be criticized on the ground that the term "improvement" is used in an elastic manner and that some of the drugs employed may control seizures only at the cost of disabling symptoms, such as drowsiness and depression in the case of bromides and phenobarbital, or at the obvious risk of severe or fatal toxic reactions, such as those with Mesantoin, phenacemide, phethenylate, trimethadione, and paramethadione. In

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From the Department of Neurosurgery, Cedars of Lebanon Hospital, Los Angeles, and the private practice of the authors.

\* References 8 and 9.

general there appears to be a consensus that phenobarbital, diphenylhydantoin, Mesantoin, and phethenylate are most effective against grand mal and that glutamic acid, trimethadione, and paramethadione are most effective against petit mal.

#### METHODS OF DRUG SELECTION

*"Standard" Method of Selection of Drugs for the Epileptic Patient.*—Without further explanation we propose to set forth here the principles which guide us in selecting medication for patients. Some of these are presented as logically self-evident; others have grown out of a long experience, and still others are based on specific investigations.

1. Relatively well-known nontoxic drugs should be preferred to dangerous or untried ones. Few fatalities have been ascribed to diphenylhydantoin, even in massive doses, and the responsibility of the diphenylhydantoin appears questionable in all those reported. A recent review of the literature is given by Chaiken, Goldberg, and Segal.<sup>13</sup> The use of phenobarbital as an anticonvulsant frequently causes drowsiness and depression but appears rarely to have fatal results, although deaths from phenobarbital poisoning, for the most part suicidal, are reasonably common.<sup>14</sup> The same is true of the use of bromides; the danger of their use is greatly decreased by close supervision. Glutamic acid is nontoxic, except that it may cause gastrointestinal irritation. Mesantoin, trimethadione, paramethadione, phethenylate and phenacemide have all been inculpated as responsible for serious poisoning and death (reviewed by Abbott and Schwab<sup>15</sup>). Doubtless the danger can be minimized by close supervision, but, as these authors have pointed out, this materially increases the patient's economic burden.

In this connection, we have not seen any dangerous toxic symptoms from Mesantoin, trimethadione, paramethadione, or phethenylate in our patients, and it appears that fewer are being reported in the literature, although the use of these drugs is expanding. It is possible that the toxic effects were due to impurities escaping removal in the early days of manufacture. We have, however, seen several cases of psychosis with phenacemide and we avoid its use whenever possible.

2. Treatment should always be begun with the most familiar, best-tested, and most reliable drug, and newer, less well-known ones should be added or substituted only for clear cause. This principle was clearly laid down by one of us (T. J. P.) in Boston<sup>16</sup> and has been admirably exemplified in an article by Yahr and associates.<sup>17</sup> Formerly phenobarbital was the generally accepted standard, but the steady success of diphenylhydantoin has caused it to become preferred. We usually start new cases on 0.2 gm. daily and increase the dose at the rate of 0.1 gm. weekly. The use of neutral diphenylhydantoin in oil (introduced by Putnam and Glaser) should not be forgotten when gastric irritation results from the use of diphenylhydantoin sodium. It is also useful for infants, in which case it must be mixed with food. Phenobarbital is our standard second choice if grand mal seizures persist. In this series several new drugs still in the stage of clinical investigation were tried when the older ones failed to give relief, but they seldom proved satisfactory (Table).

3. The dose of each new medication should be increased gradually until toxic symptoms are produced, then reduced slightly. From our experience, it is wholly clear in respect to diphenylhydantoin, and reasonably clear in regard to other

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drugs in the series, that individual needs and tolerances vary widely and cannot be predicted. Further, bitter experience has shown that it is far better to use an unnecessarily large, subtoxic dose than to run the risk of disastrous recurrence of seizures from underdosage. In many, perhaps in most, cases the effective dose is close to the toxic dose, and neither can be predicted for the individual patient.

One toxic symptom occasionally seen when diphenylhydantoin is employed, namely, hypertrophy of the gums, can almost always be controlled by vigorous massage.<sup>18</sup> Amphetamine is often useful in combating drowsiness and depression caused by phenobarbital.

Relative Effectiveness of Various Drugs

Drug	Dose, Gm.	No. of Cases in Which Used	Best or 2d in Clinical							Made Worse	"Toxic" Waves
			Best	2d	3d	4th	5th	Ineffective			
Diphenylhydantoin	1.0	29	10	6	2	1	0	8	2	0	
Mesantoin	1.0	29	3	6	7	1	2	6	3	2	
Trimethadione	2.0	27	3	5	2	1	0	8	4	1	
Phenobarbital	1.0	26	7	5	5	3	0	5	2	4	
Paramethadione	2.0	22	2	3	3	2	1	9	5	0	
Phenacemide	7.5	21	0	0	3	2	1	9	6	3	
Phethenylate	2.0	20	0	2	0	3	1	11	4	0	
Glutamic acid	30.0	18	0	2	1	0	1	14	0	0	
AC-268*	2.0	16	1	0	0	0	3	8	5	0	
Primidone	1.5	1	1	..	..	..	..	..	..	..	

Drug	Dose, Gm.	No. of Cases in Which Used	Best or 2d in Clinical			Best or 2d in Dysrhythmia Types				
			Grand Mal	Petit Mal	Psychomotor	1-2 Cps	3-4 Cps	5-7 Cps	Spike	Rapid
Diphenylhydantoin	1.0	29	16	2	6	0	6	6	2	2
Mesantoin	1.0	29	11	2	2	0	0	5	1	0
Trimethadione	2.0	27	8	1	0	2	4	2	1	0
Phenobarbital	1.0	26	10	2	3	4	2	4	0	1
Paramethadione	2.0	22	2	0	2	1	2	0	2	0
Phenacemide	7.5	21	0	0	0	0	0	0	0	0
Phethenylate	2.0	20	2	0	0	0	1	0	1	0
Glutamic acid	30.0	18	2	0	2	0	1	0	0	0
AC-298*	2.0	16	0	0	1	1	0	0	0	0
Primidone	1.5	1	..	1	..	..	1	..	..	..

\* 5-Isopropoxymethyl-5-phenylhydantoin.

4. Unless a medication under trial is clearly toxic or useless, its employment should be continued until the next drug to be tried is being given in reasonable doses.

5. The policy of increasing the dose of each drug gradually to tolerance, adding new ones to the medication if the old are inadequate, and gradually discarding those which are obviously ineffective or deleterious, should be continued until the seizures are controlled or until the available drugs have all, or substantially all, been tried. This period of trial may be shortened by the use of the method of rapid determination of optimum medication, described in this paper.

6. The use of phenobarbital, probably also of Mesantoin, is probably to be avoided at first if spike and dome or "psychomotor" complexes are present in the electroencephalogram (EEG), or in the presence of definite, typical petit mal, dulness, or psychomotor manifestations. Phenobarbital especially is apt to transform

petit mal into psychomotor attacks. The use of trimethadione, paramethadione, or glutamic acid is to be avoided at first except when some or all of these manifestations are present. When one of these latter drugs is used, it should usually be accompanied by a maximal tolerated dose of one of the hydantoins (diphenylhydantoin, Mesantoin).

7. Diphenylhydantoin, pushed to tolerance, is the drug of election in cases in which psychomotor phenomena or periodic dulness is predominant. Glutamic acid,<sup>19</sup> trimethadione, and paramethadione are next in order of preference. Amphetamine may be tried.

8. Patients should be instructed, in general, to report whenever one or a few seizures occur, and the total medication should ordinarily then be increased. This is good policy, despite the fact that the effect of an adequate dose of one or more drugs tends to increase somewhat as time goes on. In the very long run some tolerance may gradually develop and the dose may have to be increased. In growing children the tolerance should be redetermined every year or less.

9. The employment of adjuvants, such as vigorous exercise, avoidance of strain and fatigue and other obviously deleterious activities, and simple psychotherapy, is almost always advisable. Extreme moderation in the use of alcohol is imperative.

10. Surgical measures should be considered only when adequate standard medical treatment as defined, perhaps plus a trial of hyperintensive treatment† has failed.<sup>12</sup> Similar medical measures usually have to be carried out after cortical extirpations and only sometimes are more effective.

The rigid application of these principles sometimes imposes an onerous task on the physician and patient. By the application of them, however, a rate of improvement has been obtained which exceeds others reported, as has been described.<sup>21</sup> The present paper is devoted to the techniques of selection of drugs. The majority of patients are relieved promptly by taking maximal tolerated doses of diphenylhydantoin, sometimes with the addition of phenobarbital or other drugs. Patients who are not relieved as soon as the maximum tolerated dose is reached are given a trial with other medications, and their seizures are often controlled within weeks or months. In a certain proportion of cases this period of experimentation seemed intolerably, even for one or another reason disastrously, long, as will be clear in cases cited later in this paper. Under these unusual circumstances we tend more and more to a procedure which is usually called in the clinic a "drug study," but should perhaps be known as a rapid determination of optimum medication. It has been employed in 27, or 32%, of a group of 75 cases studied by us from 1947 to 1951, inclusive.

*Method of Rapid Determination of Optimum Medication.*—This method grew out of the theory, now generally well accepted but only recently so controversial, of the relationship between seizures and electroencephalographic patterns, which was first put on a sound, routine clinical basis in the former clinic of one of us (T. J. P.).<sup>22</sup> In the second place, this method rests on the observations of Lennox, Gibbs, and Gibbs<sup>23</sup> and Lennox<sup>24</sup> on the changes produced in the EEG by various medications, and on those of Schwab, Grunwald, and Sargant on the

† References 20 and 21.

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rapid normative effect of various medications on electroencephalographic abnormalities in acute experiments.<sup>25</sup> In the third place, the method was foreshadowed by the work of Ziskind and Bercel<sup>‡</sup> on the inhibition of induced changes in the EEG by various measures. As it is usually carried out at present, the method is as follows: The patient is requested to set aside approximately two weeks from work or school, during which time he lives in the hospital or is brought daily to the EEG laboratory by a relative or friend. This period should be free of engagements or obligations, for in the course of it he may have one or more seizures or may have toxic symptoms from some of the drugs employed. Usually one or the other, sometimes both, of these mishaps occur, and they are accepted as calculated risks. Since no drug is given more than once, cumulative toxic symptoms are not expected, but the doses used are maximal, and some discomfort is usually produced.

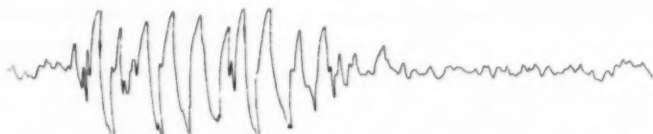
An EEG is taken as a base line after a day without medication. The patient is then given a maximal dose of one of the medications to be tried (see Table for doses usually employed), and after two hours another EEG is taken. This may be relatively brief, taken with few leads, and often without hyperventilation. He is then allowed to rest overnight (occasionally longer), then a large dose of the next drug on the list is given, and this procedure is repeated until all of the drugs to be tested have been tried. Often this period is utilized to obtain a sleep record, occasionally to make a pneumoencephalogram. In two cases the series of tests was repeated after an interval of a year or more, and in both the relative positions of the various drugs were practically identical in the second series with those found in the first. The records corresponding to the various drugs are then compared, and it is usually clear that some drugs have practically no effect, some are distinctly beneficial, and some seem actually to exacerbate the abnormalities. Sample series of records are given in the Figure.

Ordinarily all the drugs on the market are tried, usually also two or three still on an experimental basis, and often such procedures as inhalation of CO<sub>2</sub>, ingestion of glycerin, and other maneuvers which have been suggested from time to time. Sometimes, for reasons of time or economy, one or more of the drugs which have been given a thorough trial in the individual case are omitted, but this omission is probably a mistake, as the use of these drugs may afford a valuable comparison. A summary of results so far is given in the Table.

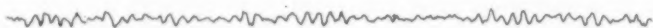
When the tests are completed and the records have been read, the patient is placed on the best, and usually also the second best, of the drugs in his series, and these are rather rapidly adjusted to a level just short of the toxic dose, according to the principles already discussed. In 21 of the 27 cases subjected to the series of tests, the medicines finally chosen were among the best three in the special tests, and this selection may be considered to represent the proportion of successes. In only seven of these cases was complete control of seizures obtained without the use of subsequent hyperintensive treatment, for only severe stubborn cases were chosen. On the other hand, there were three cases in which the hyperintensive treatment resulted in incomplete relief, but in which a subsequent rapid study indicated a change in medication which brought the seizures completely under control. Whenever possible, therefore, we carry out the rapid evaluation first. In four cases pheno-

<sup>‡</sup> References 26 and 27.

barbital showed the greatest normative effect on the dysrhythmia but was found to produce excessive toxic drowsiness, so that a second or third best had to be substituted. These cases may be considered partial successes. In seven cases none of the drugs used appeared to have much effect on the EEG pattern or were ineffective clinically. These cases were, of course, failures as far as this procedure was concerned, and most such patients were urged to undergo the narcosis, or intensive,



A. Control: Bilaterally synchronous spike and dome paroxysmal dysrhythmia sensitive to overventilation appears in a basically slower-than-normal record.



B. Primidone (Mysoline): The background for the first time became almost normal. In the third minute of overventilation, however, a gradual long seizure discharge train occurred with a rudimentary spike element. Return, however, was very prompt.



C. Phenacemide: Spike and dome bursts, short or long, before or after overventilation were absent. Instead, there were large 3 cps flat-top waves occipitally and single and double diphasic sharp waves after overventilation.



D. Paramethadione: Only rare open spikes and occipital 3 cps flat-top waves are noted, and toward the end of overventilation and thereafter scattered open spikes and 3 cps sharp waves are present. No spike and dome bursts.



E. Mesantoin: The background is more disorganized, due to intrusion of 3 to 4 cps waves, but the overventilation record shows only single spikes or single spike and dome bursts. A long seizure discharge, however, occurred after the overventilation.



F. Milontin: No spike and dome bursts appear. Bicuspid 2 to 3 cps bursts and a rare spike flurry under overventilation are the only abnormalities.

treatment. In general the procedure effected a valuable saving of time rather than supplying a new concept of treatment.

The following cases illustrate some possible indications for this elaborate procedure and the practical results, both gratifying and disappointing.



## RAPID DETERMINATION OF OPTIMUM ANTICONVULSANTS

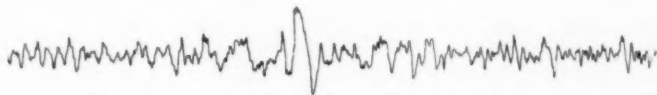
### REPORT OF CASES

**CASE 1 (B. R.).**—This 35-year-old man was first seen by us in the Cedars of Lebanon Hospital Outpatient Department in 1948. He gave the history that he had developed psychomotor seizures at the age of 19. At the time he was seen his seizures were increasing to the frequency of three times weekly. The attacks were of short duration. There was no history of birth injury or subsequent head injury. A variety of medications were tried without any benefit.

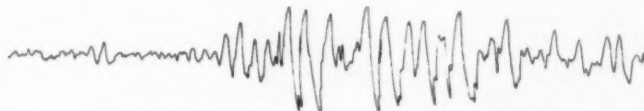
Findings on neurological examination were within normal limits except for a slightly less pronounced nasolabial fold on the left. Skull films were normal. Lumbar puncture revealed normal pressure, cell count, chemistry, and serology.



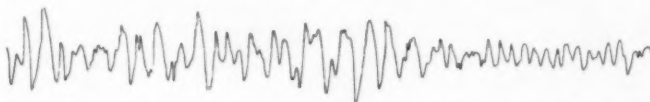
**G. Hibicon:** In fairly stable background record are interspersed rare sharp waves and open spikes, and under overventilation a single train of rudimentary spike and dome bursts.



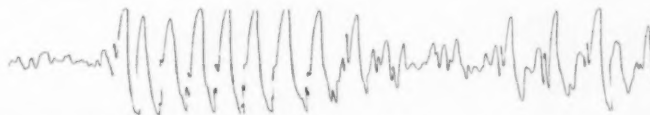
**H. Phenobarbital:** The intrusion of barbitol waves distorts the basic rhythm. Sharp waves and distorted seizure discharges, mostly single and 3 cps were seen, especially after overventilation. No spike and dome bursts were seen.



**I. Trimethadione:** This also produced a good effect on the background, but overventilation produced a series of seizure discharges early and they were more enduring.



**J. AC-268:** Very much like the Mesantoin record, but there were long spike and dome bursts during overventilation.



**K. Diphenylhydantoin:** This has all the features of the base-line record plus large (500  $\mu$ v) periodic open diphasic spikes. After 140 seconds overventilation brings out more seizure phenomena.

\* An EEG was reported as follows: "The routine record showed a dominant frequency of 9 cps and 50  $\mu$ v, mixing with one of 8 cps. A right temporal lead revealed a negative spike and slow wave with phase reversal. A positive spike was found in all these; the negative one spread anteriorly. Overventilation produced a clinical psychomotor attack, at the end of which slow waves with right lateralization were noted. Impression: This record is the commonest one found in psychomotor epilepsy."

A sleep record with anterior temporal leads was obtained and confirmation found.

The patient was brought into the hospital for rapid determination of optimum medication. This revealed that diphenylhydantoin and Mesantoin were the most effective drugs, as evidenced from the records.

The patient has now been on Mesantoin therapy for four years, during which time he has been seizure-free. He was unable to hold a position prior to this study and is now permanently at work.

**CASE 2 (D. G. S.).**—This patient, aged 2 years, had a history of retarded mental and physical development. The patient's parents gave a history of "delayed delivery." The child started to have right Jacksonian convulsive seizures at the age of 6 months. Such seizures were accompanied by a postictal right hemiplegia, which would persist for about an hour or so. These were followed with left Jacksonian seizures and grand mal seizures, occurring about once a week. Shortly after developing these major seizures he had onset of petit mal seizures, which occurred about one to five minutes daily. Simple adverse seizures, with head and eyes turned to the right, would occur about once a week.

When we saw the patient, he was taking 4.5 grains (0.3 gm.) of diphenylhydantoin daily and was ataxic, with his attacks entirely uncontrolled. He was a behavior problem, being excessively restless. A pneumoencephalogram taken seven months prior to our seeing him was reportedly normal. EEG's done at the ages of 6 and 18 months were abnormal.

Neurological examination was essentially within normal limits. An EEG revealed a very markedly abnormal record, paroxysmal and nonfocal, with slow wave and spike bursts. A sleep EEG revealed a spike and slow wave burst localized to the right temporal area and spreading to the other areas. X-rays of the skull and a pneumoencephalogram were within normal limits.

A drug study was carried out, revealing that phenobarbital was by far the best drug of all those tried. This revealed a normal sleep record. The patient was placed on phenobarbital therapy and has been completely seizure-free for two years.

**CASE 3 (J. G.).**—This case illustrates the value of a rapid, systematic determination in a patient, aged 17, who had recently had her first convulsive seizure and in whom the need for immediate control was urgent. Five months prior to her first visit she had a grand mal seizure. Her neurological examination and her skull films were within normal limits. Her EEG revealed a dominant frequency of 7.5 cps with regular 6.5 cps waves at 50 to 60  $\mu$ v interrupted by 3 cps spike and dome bursts, which were maximal in the frontal areas up to 350  $\mu$ v. Over-ventilation in 140 seconds produced at first similar seizure discharges. Two weeks later 3 cps parieto-occipital waves were added.

A comparative study was done. Primidone (Mysoline) improved the record more than any other drug but did not prevent one terminal seizure discharge after overventilation. Trimethadione behaved similarly, but there was more reaction to overventilation. Paramethadione, Hibicon (*N*-benzyl- $\beta$ -chloropropionamide), Milontin (methylphenylsuccinimide), and phenacetamide, in that order, failed to normalize the background tracing entirely. Under overventilation all these drugs distorted and broke up the typical short and long spike and dome discharges. Paramethadione made the patient nauseated. Phenobarbital produced the most distortion of extraneous origin. The other drugs hardly altered the premedication record.

This young woman has now been followed for one year five months and has been seizure-free on primidone, 1 to 1.25 grains (65 to 80 mg.) daily. The figure illustrates the comparative strips of this patient's records. It is obvious that Record B, with primidone, was the best record obtained.

#### COMMENT

From the practical point of view, this procedure has obvious advantages and disadvantages: (a) It is rapid and affords an objective evaluation. On the other hand, it is expensive. (b) It entails considerable incapacity and discomfort while it lasts, and the results are still not of assured value to the patient. (c) It cannot be used at all unless there is a definite, fairly persistent dysrhythmia. Perhaps it is more significant in indicating the drugs or measures to avoid than in selecting immediately the optimum.

## RAPID DETERMINATION OF OPTIMUM ANTICONVULSANTS

Even the few results tabulated here are capable of teaching us something about the relative value of different drugs. It is clear at a glance that no single one is "best," although one or another is often obviously preferable for the individual patient. This fact in itself is sufficient justification for continued efforts to find new anticonvulsant compounds, even though they do not displace the standard ones.

The results of this study fail to bear out some clinical impressions. As will be seen from the Table, phenobarbital was effective in diminishing slow wave complexes in 10 out of 26 cases in which it was tried. Trimethadione appeared to have an excellent normative effect on the dysrhythmia in eight cases in which the predominant attacks were of the grand mal type.

Diphenylhydantoin made the best showing, a surprising finding considering that with few exceptions only patients who did relatively poorly on it in previous clinical trials were subjected to the series of tests. Phenobarbital stands near the top of the list but could seldom be used as the chief component of the combination finally elected because of the drowsiness it produces. It is curious how closely the relative effectiveness of the drugs employed follows the historical order in which they were introduced.

The objectivity and clarity of this method recommends it as a procedure of early choice in evaluating new drugs after due experiments in animals.

Obviously, many variations might be made in the method. The dosages were chosen rather arbitrarily, chiefly on the basis of the average maximum tolerated. The period of disability might be shortened by giving one new drug each week end, omitting those which were unsatisfactory on clinical trial. Possibly further experience will show that drugs may be arranged into groups, which may be discarded as a whole if one member seems ineffective or deleterious. The use of frequency analysis would doubtless add to the accuracy of the procedure, but even as it stands it appears to possess practical usefulness.

### SUMMARY AND CONCLUSIONS

A method is described which permits a rapid, though expensive and rather disagreeable, method of evaluating anticonvulsant drugs in patients suffering from various types of seizures. Its disadvantages are such that it should find use only under special conditions, in patients not promptly relieved by "standard" treatment. In the past five years (to 1953) it has been employed in 27 out of the 75 patients treated.

The method consists in administering the drugs to be tested in series, approximately one a day, in maximal tolerated doses. After each dose has had an opportunity to exert its maximal effect, an EEG is taken. A comparison of the records usually shows quickly which drugs are preferable and which are likely to prove disadvantageous, in each patient tested.

The results of this investigation show clearly that there is no single "best" drug for the treatment of epilepsy.

In the resistant, difficult cases submitting to these tests, sometimes no drug was found particularly effective. The most effective drug in the test was sometimes poorly tolerated by the patient. With few exceptions, however, those drugs which did not improve the EEG abnormalities, or which made them worse, were ineffective or deleterious, so that the field of choice was correspondingly narrowed.

The use of this method may save much time, even years, of experimentation to determine the medication required to keep the individual patient seizure-free or as well as possible. It probably does not improve the end-result, as compared with the standard method of trial and error.

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## EFFECTS OF CASTRATION ON HYPERSEXUAL BEHAVIOR INDUCED BY RHINENCEPHALIC INJURY IN CAT

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CONTRIBUTIONS to our knowledge on the role of neuroendocrine mechanisms in the regulation of sexual behavior in mammals have been carefully summarized and evaluated in two excellent reviews by Beach.\* It is generally agreed that copulatory behavior of adult males of several subprimate species can be diminished by castration or by injury of the central nervous system.

The observations of Beach and Zitrin† indicate that extensive but incomplete destruction of the neocortex markedly interferes with the coordination of sensory-motor components of coital behavior in male cats. After complete neocortication their cats failed to exhibit sexual interest or overt patterns of mating behavior when placed in association with receptive females. From these findings it would seem that the neopallium of this male carnivore, in addition to contributing sensory-motor components, exerts a generalized facilitative influence upon subcortical structures involved in the mediation of sexual behavior.

In addition to contributions from the neopallium, patterns of sexual behavior are also regulated to some extent by neural influences mediated by the archipallium. Several investigators‡ have described pronounced and durable increases in sexual activities of rodents, carnivores, and primates sustaining lesions of the forebrain limited largely to the rhinencephalon. In a recent publication<sup>§</sup> we described markedly augmented copulatory behavior exhibited by male cats with rhinencephalic lesions primarily restricted to the amygdaloid nuclei. Such findings indicate that these neural structures serve, in part, to inhibit or otherwise moderate the frequency and intensity of overt sexual behavior of this subprimate species. The study was subsequently extended to include the effects of castration and androgen therapy upon hypersexual behavior induced by rhinencephalic injury in the male cat, the results of which are presented in this communication.

### METHODS

Fourteen adult male cats sustained bilateral lesions of the rhinencephalon after varying periods of observation had established their desire to manifest copulatory behavior upon female and male cats, agoutis (*Dasyprocta agouti*, a large Central American rodent), dogs, monkeys, and chickens. Lesions were made by aspiration, utilizing the approach and surgical technique described in previous communications.<sup>§</sup>

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\* References 1 and 2.

† Beach,<sup>1</sup> pp. 259-260.

‡ References 3 through 6.

§ References 5 through 7.

## CASTRATION—EFFECTS ON HYPERSEXUAL BEHAVIOR

Two of the 14 cats were castrated two weeks prior to, and 4 were castrated at the time of, placement of the rhinencephalic lesions (Group II). The remaining eight amygdalectomized animals (Group I) were observed for periods of 2 to 12 months before castration.

In the postoperative periods all preparations were given repeated access to receptive females of their species, to one another, and to agoutis, dogs, monkeys, and chickens. During such periods the presence, nature, and intensity of male and female sex behavior displayed by the animals operated on were observed and recorded. After castration the animals comprising Group I were separated into two subgroups. Subgroup A (four animals) received a daily intramuscular injection of 50 mg. of testosterone propionate U. S. P., beginning approximately three weeks after gonadectomy and continuing for periods ranging from three days to two weeks. During comparable periods the four untreated animals comprising Subgroup B served as controls.

Several females, maintained in a highly receptive state by the administration of diethylstilbestrol after oophorectomy, and additional amygdalectomized, but otherwise intact, males served as stimulus animals on several occasions throughout the study.

At the termination of the observation periods the preparations were killed, and the brain of each animal was sectioned and stained for histological evaluation of the extent of the lesions. The accompanying figure contains serial tracings and photomicrographs of sections at various levels through the rhinencephalic lesions sustained by a behaviorally typical cat of Group I. Additional anatomical data are included in a previously published report.<sup>6</sup>

### RESULTS

*Preoperative Sex Behavior.*—Over periods from 10 to 120 days, each of the 14 experimental animals was repeatedly placed in free association with anestrus and estrous female cats, other male cats, agoutis, dogs, monkeys, and chickens. Their behavior in these situations was carefully observed and recorded.

In the presence of males and anestrus females of their own species, the experimental animals at times displayed mutual grooming and other contact behavior. In no instance, however, did such association lead to copulation. Activities pursued by the 14 male cats when confronted with animals of other species, particularly dogs and monkeys, consisted almost entirely of escape and fighting behavior.

In the presence of highly receptive females of their own species (receiving diethylstilbestrol after oophorectomy), the cats engaged in extensive courtship maneuvers, which included licking and other nonmounting contact. In some instances such maneuvers culminated in mounting and intromission. Some experimental animals, when sufficiently aroused by receptive females, were seen to make overt sexual advances upon other male and nonreceptive female cats, which, however, responded with snarls, hisses, and attacks with teeth and claws. Such reactions were sufficient to suppress further sexual pursuit.

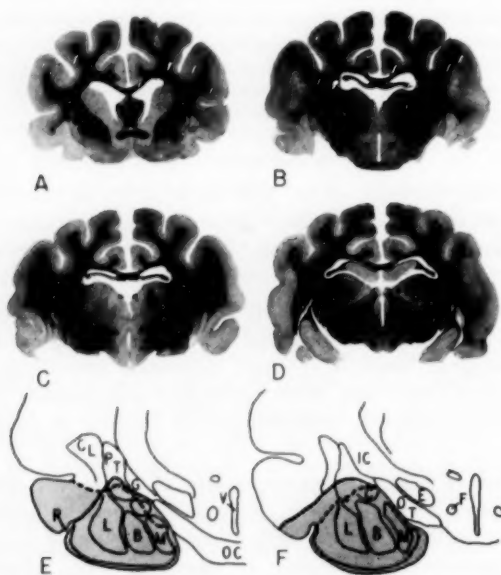
*Postoperative Sex Behavior.*—During their postoperative survivals the two preparations which were castrated two weeks prior to placement of rhinencephalic lesions and the four animals which sustained simultaneous bilateral gonadectomy and amygdectomy, all of Group II, at no time demonstrated male copulatory behavior. When placed in association with unfriendly animals of other species, the cats remained placid and displayed markedly reduced activities of escape, defense, and aggression. They did, however, exhibit considerable interest in other animals, as demonstrated by frequent oral and other related physical contact. When placed in association with estrous females of their own species, these preparations were friendly and solicited extracoital contact, but in no instance were they seen to display male copulatory behavior. They did, however, exhibit some



elements of feminine copulatory behavior, as described in a subsequent section.

Increased sexual activity was the most prominent behavioral alteration observed in the eight amygdalectomized but otherwise intact animals (Group I). Within the second to the fourth postoperative week mating patterns, usually associated with precoital sex play, became very pronounced. These included increased motor and investigative activity, marked restlessness, and exaggerated oral and vocal behavior. Within a few days after the appearance of these changes vigorous copulatory behavior was added.

When placed in unrestricted association with estrous females of their species, the preparations exhibited minimal precoital sex play, mounted rapidly, and achieved intromission in very short periods of time. Given access to females



Sections taken at various levels through brain of Cat 54. Section *A*, immediately rostral to lesions; Sections *B* and *C*, through greatest extent of lesions; Section *D*, through caudal aspect of lesions. Diagrams *E* and *F* illustrate extent of lesions in Sections *B* and *C*, respectively. Stippled areas below heavy solid lines represent lesions on left side. Stippled areas below heavy broken lines represent lesions on right side. Abbreviations are as follows: *B*, basal amygdaloid nuclei; *C*, central amygdaloid nuclei; *CL*, claustrum; *E*, entopeduncular nucleus; *F*, fornix; *G*, globus pallidus; *IC*, internal capsule; *L*, lateral amygdaloid nuclei; *M*, medial amygdaloid nuclei; *OC*, optic chiasm; *OT*, optic tract; *PT*, putamen; *R*, rhinal sulcus; and *V*, third ventricle. (This figure originally appeared in the *Journal of Neurophysiology*<sup>6</sup> and is here reproduced with permission of the editors.)

made highly receptive by daily administration of diethylstilbestrol after oophorectomy, the amygdalectomized males mounted and achieved intromission, occasionally as often as three or four times in one hour. Such activity was observed daily throughout their precastration periods, which ranged from 2 to 12 months.

Copulatory activity was also the dominant feature of behavior exhibited by the animals of Group I when in the presence of males and females of other animal species. Rather friendly dogs and monkeys were invariably mounted, and vigorous

copulatory activity ensued. During periods in which the dogs or monkeys became hostile and attacked, the amygdalectomized cats showed no evidence of fear and tenaciously hung onto their partners with seeming determination. Similar sexual advances were made upon 2-week-old kittens, agoutis, and chickens.

Several cats of Group I were given access to inanimate animal-like objects. On two successive days and in several trial periods of approximately 10 minutes' duration, none of the preparations were seen to mount a cat-sized plastic horse or a small, fuzzy Teddy bear.

*Effects of Nonsexual Stimuli.*—Sexual arousal and mating behavior of animals of Group I were not inhibited by stimuli which are usually thought to be non-sexual in nature. As previously described, they were not deterred from carrying out copulatory activities upon rather unfriendly dogs and monkeys, which at times became sufficiently aroused to exhibit savage behavior. On several such occasions the cats were clawed and bitten. After releasing the neck grasp, dismounting, and retreating a few steps, the cats would immediately remount and pursue activities in which they were engaged prior to the disruption. Such behavior in alley cats not operated on, if ever displayed, is unusually rare.

In addition, these eight amygdalectomized cats showed no hesitancy in displaying copulatory behavior in strange surroundings. Various test areas, which included the cages of dogs, monkeys, and agoutis, other animal quarters in which a number of barking dogs were housed, the operating room, classrooms, and the investigators' private office, were of no hindrance to the sexual habits of these cats. In addition, rather high room temperatures and the intense illumination required to obtain cinematographic records<sup>6</sup> were also compatible with unrestrained copulatory behavior with animals of other species.

Stroking and petting served to heighten the sexual interests of the Group I cats in that they repeatedly and harmlessly grasped with their teeth the loose skin of the observer's hand in a fashion strikingly similar to that taken by them upon another animal. On such occasions they became very restless, vocalized, licked, rubbed their flanks against the experimenter's arm, and exhibited jerky movements of their backs and tails. Handling these animals upon the laboratory floor was a full-time job because of their persistent attempts to sneak away in order to mount and copulate with animals standing nearby. When such a situation arose, grasping a mounted, amygdalectomized male by the loose skin of his shoulders did not deter him from his sexual pursuits in that he would hang onto his partner even when both animals were suspended in mid-air.

*Bisexual Mating Behavior.*—The eight amygdalectomized but otherwise intact cats comprising Group I exhibited female, as well as male, mating behavior. Previous paragraphs described them as unusually vigorous copulators when placed with receptive females of their species. Pairing these amygdalectomized males brought forth considerable sex play in which they alternately took the neck grasp, mounted, and executed pelvic thrusts upon each other. Males in the conventional feminine position were tolerant of the mounted males in that they remained in crouched, rather motionless positions, which on occasions included slight lordosis. After a short period of time the relative positions of the paired animals would become reversed, and comparable mating behavior would ensue.

When several animals of Group I were allowed access to one another, similar sexual activity became manifest. During such instances, however, it was not unusual to observe four or five males mounted one upon the other, in tandem fashion, each maintaining the neck grasp and executing pelvic thrusts upon his more dependently located associate. During such maneuvers, therefore, each animal executed male copulatory behavior upon his partner below while simultaneously serving as a female stimulus animal for his partner above.

Because of the decreased latency and increased frequency of copulation with receptive females and the pronounced willingness to attempt copulation with male cats and all available animals of other species, the amygdalectomized cats comprising Group I were considered to be extremely hypersexual in character. This, then, was the nature, intensity, and background of male copulatory behavior upon which the effects of castration were observed.

*Effects of Castration.*—Two to 10 months after the previously described patterns of hypersexuality had reached a markedly elevated and stable plateau, the animals of Group I, all of which exhibited such behavior, were castrated. During the first postoperative day their sex drives and copulatory activities in the presence of males and females of their own and other species were comparable in every respect to those displayed by them in their precastration periods. Beginning on the second or third day, however, their persistence in sexually attacking cats of either sex, as well as members of other animal species, began to wane. Although the castrated males continued to mount all available animals, the frequency and intensity of their total copulatory patterns decreased, and non-copulatory sex play became more prolonged. Failure of the preparations to mount and execute pelvic thrusts upon dogs, monkeys, agoutis, and chickens represented the first unquestionable indication of their decreasing sexual interests. Gradually, all forms and phases of mating behavior became less intense, and after the 7th to the 10th postcastration day no overt male copulatory behavior and very little noncopulatory sex play were exhibited by them when placed in daily association with receptive females of their species.

Postoperatively, all cats of Group II (castrated either prior to or at the time of bilateral amygdalectomy) were repeatedly placed in test situations conducive to the display of sexual behavior. Throughout their survivals they remained extremely docile, exhibited increased oral and investigative activity, were friendly to animals of their own and other species, but in no instance displayed male copulatory behavior. The presence of receptive female cats did not arouse these six preparations to take the neck grasp, mount, or carry out pelvic thrusts. They simply remained friendly, sexually disinterested animals which seemingly served as sources of unending disappointment to receptive females of their species.

*Feminine Mating Behavior.*—It is recalled that two cats of Group II were castrated approximately two weeks prior to injury of the rhinencephalon. In the interim between their pelvic and cranial surgery, these animals were repeatedly allowed to associate freely with animals of Group I, all of which displayed exceptionally strong sex drives. Mounting and other copulatory behavior thrust upon the castrates by the highly aroused, gonadally intact animals of Group I was not tolerated. When such situations arose, the castrates withdrew or otherwise freed themselves from serving as female sex targets. After bilateral amygdalectomy,

however, these two preparations and the remaining four animals of Group II (castrated and amygdalectomized in one stage) displayed marked tolerance for male copulatory behavior carried out upon them by animals of Group I. This feminine-like mating behavior, which at times included elevation of the pelvis and lateral deviation of the tail, was demonstrated more clearly by animals of Group II than was demonstrated by members of Group I after castration, as related below.

As described in a previous section, feeble but seemingly significant female mating behavior was exhibited by animals of Group I. After castration and ultimate disappearance of all male copulatory behavior, however, these animals demonstrated increased tolerance for copulatory activities performed upon them by hypersexual males which were prepared for another study and available to serve as stimulus animals. When mounted, the Group I castrates crouched, remained relatively motionless, and calmly served as recipients of pelvic thrusts. In many instances they responded to such stimuli by assuming a lordotic stance.

*Effects of Androgen Therapy.*—Approximately 10 days after all evidence of male copulatory behavior ceased to be exhibited by the eight castrated animals comprising Group I, four received daily intramuscular injections of 50 mg. of testosterone propionate (Subgroup A). After a few days each of these animals displayed a pronounced increase in sex play, and within the second week of androgen therapy patterns of hypersexual behavior had reached their precastration levels. The range of animal species to which the cats reacted sexually was also as wide and varied as that present before castration. Throughout comparable periods the behavior of the four untreated animals (Subgroup B) remained unchanged.

#### COMMENT

The rapid decline in male copulatory behavior after gonadectomy (Group I animals) and the failure of the amygdalectomized castrates (Group II) to exhibit masculine mating patterns suggest that the increased sex drive displayed by animals of Group I was dependent for expression upon influences of testicular origin. The subsequent return of male copulatory behavior to high levels after the administration of testosterone propionate (Subgroup A) provides evidence that hormonal secretions of the testis are responsible for maintenance of the state of chronic hypersexuality in the adult cat that follows injury of the rhinencephalon largely limited to the amygdaloid nuclei.

These findings do not imply that all copulatory behavior of the normal or amygdalectomized male cat can be abolished by castration. While the amygdalectomized castrates soon failed to display mounting and all other male copulatory behavior, they might well have been fully capable of it. They did, however, engage in precoital sex play and demonstrated female mating behavior which was more pronounced than that displayed in their precastration periods (Group I). This augmentation could have been a manifestation of the increased placidity, general lethargy, and reduced motor activity which followed gonadectomy. On the other hand, this increase in female mating behavior might have resulted directly from the removal of testicular influences which normally excite neural mechanisms to elicit patterns of sexual behavior primarily of the male type.

Such neural mechanisms, however, are less clearly defined. Contributions from the neocortex serve to facilitate the arousal and execution of copulatory activity by the male cat.<sup>1</sup> On the contrary, paleocortical influences appear to suppress the frequency and diversity of mating behavior, since lesions of the rhinencephalon precipitate a chronic state of hypersexuality.<sup>||</sup> Released from suppression, therefore, subcortical structures, including the hypothalamus,<sup>¶</sup> hypophysis,<sup>#</sup> and brain stem,<sup>11</sup> are facilitated by neocortical influences in the integration and elaboration of increased sexual responsiveness exhibited by the amygdalectomized, adult male cat.

#### SUMMARY

Lesions of the rhinencephalon, largely limited to the amygdaloid nuclei, precipitate a state of chronic hypersexuality in the adult male cat. Such behavior is abolished by castration. It is maintained, therefore, by endocrine secretions of the intact testes, since after gonadectomy the daily administration of 50 mg. of testosterone propionate restored the hypersexual behavior to precastration levels.

Some neuroendocrine relationships bearing upon these findings are discussed. Ablation of rhinencephalic structures appears to release from suppression certain subcortical structures which, together with neocortical influences, contribute to the initiation and maintenance of hypersexual behavior displayed by the gonadally intact, adult male cat.

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¶ References 6 and 8.

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## OCCLUSION OF THE CAROTID ARTERIES

### Further Experiences

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IN AN EARLIER paper<sup>1</sup> the broad problem of occlusion of the cervical portion of the internal carotid artery was discussed in the light of knowledge existing at that time, and the prediction was made that it would prove to be of major importance in the study of cerebrovascular disease. During the past two years the cervical portion of the carotid arteries has been studied routinely at autopsy, and the results show clearly the validity of this prediction. The cases examined have included not only many instances of cerebrovascular accident but many cases serving as controls. The need for such a clinicopathological study was clearly indicated on two counts: In the first place, a full pathological examination has almost never been made in the recorded cases of carotid occlusion diagnosed by arteriography. Moreover, the cases of carotid occlusion which reach the neurosurgical clinic are usually highly selected, and a true picture of the disease is not encountered there. Secondly, in Hultquist's<sup>2</sup> extensive pathological study little or no attempt was made to correlate clinical data with the anatomical findings.

In the relatively short period of this study 45 cases of occlusion of one or both carotid systems have been found. In the great majority of the 45 cases complete occlusion was present, but a few others are included because, although a pinhole lumen remained, there were associated signs and symptoms. An additional 13 cases showed extremely severe stenosis of one or both sides, unassociated with abnormal clinical or pathological findings. Four instances of cerebral emboli breaking away from mural thrombi deposited upon atherosclerotic ulceration within the carotid sinus have also been found. This paper is a survey of the general clinicopathological features in all these cases.

### MATERIAL

Almost all cases were from the wards of the Montreal General Hospital and St. Anne's (Veterans) Hospital. The former is a large, unrestricted, adult-receiving hospital, so that autopsy material was largely unselected. There, in 432 consecutive routine autopsies in which the brain was examined the cervical portion of the carotid arteries was removed for study. The intracranial portion of the vessel was also removed in most cases, but no attempt was made to examine the section within the petrous bone routinely, as Hultquist had found this region rarely affected. The cases were adults of all ages and from both the medical

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and the surgical services. Of the 432 routine cases, 28 (6.5%) had complete occlusion of one or both carotid arteries, and an additional 13 showed very severe narrowing of the arterial lumen; that is, approximately 9.5% had advanced carotid disease. This incidence is much higher than Hultquist reported and may depend on the fact that the recent introduction of antimicrobial agents has resulted in a reduction of deaths due to infection and an increase in the number of cases in which atherosclerosis has been able to run its full course. St. Anne's (Veterans) Hospital is devoted to the care of chronically disabled veterans of the Canadian armed services, and many are patients because of cerebrovascular accidents. In one and one-half years 17 cases of carotid occlusion came to necropsy at this hospital.

Table 1 shows the incidence of other cerebrovascular diseases in the 432 unselected cases. More than one-half had evidence of vascular insult, an unusually

TABLE 1.—Incidence and Type of Vascular Disease in 432 Unselected Autopsies

	No.
1. No significant vascular disease.....	214
2. Occlusion of one or both carotid arteries.....	28
3. Severe stenosis of carotid artery (probably not significant).....	13
4. Cerebral embolism.....	55
5. Hypertensive atherosclerotic encephalomalacia (lacunae).....	31
6. Cerebral hemorrhage.....	32
7. Lesions 5 and 6 combined.....	13
8. Ruptured "berry" aneurysm.....	9
9. Indeterminate.....	15
10. Thrombosis of basilar artery.....	3
11. Thrombosis of posterior cerebral artery.....	2
12. Thrombosis of other major vessels.....	7
Vertebral.....	4
Posterior inferior cerebellar artery.....	1
Multiple.....	2
13. Dural hematoma.....	4
14. Miscellaneous—neurosyphilis, occlusion of posterior communicating artery.....	6
	432

high figure and one which warrants the attention of physicians interested in the neurological ills of older people. No further explanation of the various diagnoses is needed except to say that the term "hypertensive atherosclerotic encephalomalacia" is used here to refer to *l'état lacunaire*, which correlates very highly with the presence of both hypertension and atherosclerosis. It will be noted that thrombotic occlusion of major vessels adjacent to the circle of Willis was seen only 12 times in the total of 218 cases with vascular lesions. In contrast, carotid disease was found 41 times, that is, with about the same frequency as that of cerebral hemorrhage and hypertensive atherosclerotic encephalomalacia, and with a frequency somewhat less than that of cerebral embolism. These figures serve to place carotid disease clearly in its proper perspective within the general field of cerebrovascular disease.

## CLINICAL AND PATHOLOGICAL FEATURES

First of all, it is necessary to point out that the final spectrum of clinical manifestations following upon carotid disease has yet to be formulated. Prior to arteriography there had gradually grown up the classical clinical concept of



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thrombosis of the internal carotid artery, namely, monocular optic atrophy and blindness associated with contralateral hemiplegia. That this was much too narrow a concept was shown soon after the introduction of arteriography, but, in turn, the clinical picture as determined by reports from neurosurgical clinics has remained a very incomplete and unrepresentative one, for arteriography as noted above would be entertained as a diagnostic procedure only when the history and physical examination suggest an expanding intracranial lesion. My previous report drew attention to the presence of carotid disease in what might be termed "ordinary strokes," and it has become apparent that the problem of carotid disease, especially its incidence and the scope of its clinical pattern, demands an extensive revision of the neurosurgeon's concept. At the present time, after a clinical and pathological study of 45 cases, there would appear to be an extremely rich and varied symptomatology whose full range is still not clearly in view. The more general clinical features are seen at a glance in Table 2, and further details will be added in the comment at the end of each group of case presentations.

TABLE 2.—*Classification of the Clinicopathological Features in Forty-Five Cases of Carotid Occlusion*

1. Unilateral occlusion without symptoms.....	7
2. Unilateral occlusion with hemiplegia.....	20
3. Unilateral occlusion with symptoms arising during shock or anoxia.....	7
4. Unilateral occlusion associated with dementia.....	8
5. Bilateral occlusion with bilateral neurological signs and coma.....	6
6. Bilateral occlusion with dementia.....	5
7. Embolus arrested at bifurcation of common carotid artery.....	3
8. Cerebral embolus arising from mural thrombus within the carotid sinus.....	4
9. Cerebral embolus arising distal to severe stenosis.....	5
10. Miscellaneous .....	3

On the pathological side the picture is also complicated, for in many cases only the scars of ancient processes are found and it is with difficulty that past events are reconstructed. In addition, there is great variability with regard to the site of occlusion, the extent of secondary thrombosis, the occurrence of embolization, the efficiency of the collateral circulation, and the size of the cerebral softening. In spite of the pathological complexity, it is advantageous to classify the present series of cases, first, according to the pathological picture and, second, according to the broadest clinical features.

The classification shown in Table 2 has been adopted, and the incidence of each group is shown. Of course, one case can qualify for more than one group; for example, a case of dementia might terminate with a fatal hemiplegia, or a patient with unilateral occlusion associated with hemiplegia might survive, to die later of occlusion of the remaining side.

Before we proceed with a presentation of representative cases from each group, a few of the most important neuropathological aspects of the problem must be briefly discussed. The substrate of carotid occlusion, in most cases, is atherosclerosis. There is a special tendency for atherosclerotic deposits to be made within the carotid sinus at the origin of the internal carotid artery (Fig. 1). The striking size of some of these plaques is always startling to anyone seeing them for the first time. This herald plaque may enlarge to the point of virtually occluding the lumen of the artery, or occlusion can result from superimposed thrombosis, or

perhaps hemorrhage into the plaque. It is often difficult even on microscopic examination to determine the exact constitution of the occluding mass, and at times it is quite impossible to distinguish an old embolic plug from a thrombus formed in situ.

It is commonest in cases of hemiplegia to find secondary thrombosis within the internal carotid artery distal to the blocked sinus, this secondary thrombosis extending up into the cavernous portion and even into the middle and anterior cerebral arteries. If death does not result, the blood clot within the artery becomes organized and in time the artery is reduced to a small solid cord, in which the vessel wall can be recognized surrounding a pale yellow core. During the process the clot progresses through all the shades of color which extravasated blood shows as it is removed in the healing process. The presence of severe atherosclerosis within the carotid sinus and a clot or cord distal to it allows one to conclude that the primary occlusion was at the sinus and that the change in the distal portion

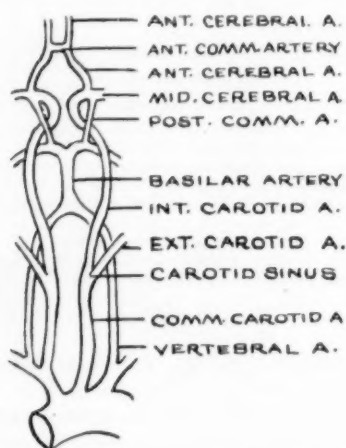


Fig. 1.—Diagram showing the carotid arteries in their relation to the aorta, the circle of Willis, and the basilar system. The carotid sinus is the site of predilection for atherosclerotic deposition.

of the internal carotid artery was secondary. However, in four cases the internal carotid artery was either reduced to a cord or distended by a recent antemortem thrombus, when the sinus did not show occlusive atherosclerosis. In these cases it would seem that the primary closure was intracranial (in the cavernous sinus, in the siphon, or at the bifurcation of the internal carotid artery) and retrograde thrombosis had occurred back to the region of the carotid sinus. In one of these cases advanced atherosclerosis was found just proximal to the bifurcation of the internal carotid artery, but in the others no definite blockage which might have precipitated the intravascular clot was discerned. Hultquist found primary occlusion of the internal carotid to occur in two-thirds of cases at the sinus and in one-third of cases near the origin of the ophthalmic artery. This proportionate distribution is not corroborated in the present series, but it is likely that Hultquist's examination in situ provided more reliable data than the present series, where the intracranial portion of the artery was dissected free for later examination.

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Several other types of pathological picture have also been encountered. In two cases not only was the internal carotid artery reduced to a cord but the common carotid artery on the same side was similarly affected down to its origin from the innominate or aortic vessels. In these cases retrograde thrombosis had probably proceeded proximally from the region of the sinus, the external carotid artery also becoming blocked at the same time. In three cases a large embolus had become lodged at the bifurcation of the common carotid artery, leading to hemiplegia each time. In at least three additional cases an embolus may have served to precipitate carotid thrombosis some time previously, but in the healed stage the nature of the pathogenesis cannot be determined, particularly if the degree of carotid atherosclerosis is such that it, too, might have been a factor. In this series cases of embolism to the bifurcation of the internal carotid artery intracranially are not included, for these would be recognized in routine postmortem examination, and one of the purposes of this paper is to emphasize that examination of the cervical portion of the carotid vessels is absolutely essential in many cases to achieve an accurate clinicopathological correlation. The correct diagnosis in most of the cases in this series could have been made only by study of the vessels in the neck.

The atherosclerotic plaque within the carotid sinus is prone to ulcerate, and mural thrombus is often found deposited thereon. A cerebral embolus arising from such a mural thrombus was found in four cases. Chiari<sup>3</sup> pointed out this chain of events some 50 years ago, but his lead was not followed up. Another very important pathological variation, namely, cerebral embolus arising distal to an extremely stenosed carotid artery, was found in five cases. In one of these, marked by hemiplegia, the lumen at the sinus was narrowed to 0.5 mm., while on the same side a good-sized cerebral embolus was found occluding the anterior cerebral artery. This embolus was too large to have passed through the narrowed portion of the carotid sinus, and it was concluded that the embolus formed distal to the point of narrowing in the carotid sinus. This possibility is of great importance, for it no doubt is one of the mechanisms by which an incompletely occluded carotid vessel can produce a hemiplegia. In such cases examination months later will show no vessel occlusion intracranially, for the embolus, as a rule, will have long since disintegrated and disappeared.

Bilateral carotid disease adds further complexity to the pathological picture. No less than 10 cases fell within this category. Five of these were associated with "senile dementia," and it would appear that in the long history of the study of senile dementia the state of the carotid vessels carrying the major portion of the blood supply to the brain has never before been investigated.<sup>4</sup> In three others there had been occlusion of one side and a resultant hemiplegia a few years previously, and finally, when the other carotid artery became thrombosed, bilateral neurological signs and coma resulted. Three patients had had a "silent" occlusion on one side and manifested bilateral signs and coma only when the other side became blocked—in two by thrombus, in the other by an embolus.

It was pointed out above that the carotid sinus was the site of predilection for atherosclerosis. This is certainly true in most cases, but four exceptions occurred. In three cases the left common carotid artery near its origin from the aorta was virtually occluded by a very large plaque, and if the carotid system had not been examined in its entire cervical extent (including the arch of the aorta), the lesion

would have been missed. The other case showed an occlusive plaque in the common carotid artery 2.5 cm. proximal to the region of the sinus. It is a significant fact that the carotid vessels in the neck may show extensive occlusive disease, and yet the intracranial vessels themselves be free, or almost free, of atherosclerosis. Thus the importance of examination of the cervical vessels is again made plain. Upon routine removal of the brain at necropsy, a clue that one is dealing with cervical carotid occlusion is furnished by an unusual smallness of one internal carotid "stem" or by the presence of a dry blood clot, distending the internal carotid artery where it is sectioned for the purposes of removal of the brain.

The atherosclerotic process seen in the region of the carotid sinus was typical of the disease as it occurs elsewhere in the body, and in the present material never resembled thromboangiitis obliterans. A most interesting finding, and one of some theoretical importance, was the complete absence of subintimal atherosclerotic deposits in the stretch of internal carotid artery between the sinus and the base of the skull, no matter how markedly affected the sinus might have been. Hemorrhage within a plaque was common, and mural thrombus deposited upon atheroma was not rare. Foreign body giant cells were seen at the site of an atherosclerotic ulcer in one case. Degeneration of the medial layer of the wall of the sinus (Erdheim's medial necrosis) with local dissection occurred in one instance, while in another the carotid sinus was partially obstructed by a section of aortic wall which had broken away from a dissected region of the arch of the aorta.

The pathological changes in the brain itself varied a great deal. On one hand, the brain could be quite normal grossly and microscopically in patients entirely without symptoms. In cases of hemiplegia of short duration in which the internal carotid artery was filled with recent blood clot, there was softening of the hemisphere to a degree dependent on such factors as the distance distally to which the clot had extended, the form of the circle of Willis, and the adequacy of the collateral circulation. When an embolus had arisen from a mural thrombus or arose distal to a region of stenosis, the cerebral softening was quite characteristic of the embolic process under more usual circumstances. Sometimes small old focal lesions in the basal ganglia were the only changes to be attributed to a long-standing carotid occlusion.

An uncommon type of softening which has previously remained unexplained proved to be due to occlusion of the internal carotid artery. I refer to "watershed infarction," in which the most peripheral adjacent territories of the middle and anterior central arteries are extensively softened, the more proximal regions being intact. This process results in a long narrow infarct reaching almost from the frontal to the occipital pole, lying along or near the superomedial angle of the involved hemisphere. In cases of bilateral occlusion with bilateral symptoms and signs both cerebral hemispheres usually showed softening. The mechanism of this widespread bilateral infarction has heretofore not been evident. The importance of examining the carotid vessels before making a clinicopathological correlation was especially well illustrated in one case in which the patient had had auricular fibrillation complicated by a recent hemiplegia. On pathological examination a cerebral softening was found, along with embolic material within the supplying vessel. The tentative conclusion was that of cerebral embolus arising from a diseased heart; yet, the internal carotid artery on that side showed an old, well-

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organized occlusion, which, in conjunction with the form of the circle of Willis, made it impossible for an embolus to have reached its site of lodgment from a cardiac source.

Another complicating factor, especially in making an accurate clinicopathological correlation, was the occurrence of unrelated vascular disease, either thrombosis or embolism, in other regions of the brain. This was not uncommon, there being one case of thrombosis of each of the following arteries, basilar, vertebral, anterior cerebral, and posterior cerebral, while three cases of embolism and two cases of hypertensive softening were also found. One further point remains, namely, the difficulty in assessing simple narrowing of the carotid lumen without occlusion. I have arbitrarily concluded that narrowing of the caliber of the vessel to 0.5 mm. is significant, especially if both sides are affected. When it is recalled that flow in a tube varies as the fourth power of the radius, it is highly likely that a significant decrease in blood flow occurs long before the lumen is narrowed to 0.5 mm. It is clearly impossible to reach a conclusion in the matter without physiological studies of the cerebral blood flow in such patients.

### PRESENTATION OF REPRESENTATIVE CASES FROM EACH GROUP

1. *Unilateral Occlusion Without Symptoms.*—In this category there were seven cases, a few of which will be described.

Case 1 was that of a man aged 74 who died as a result of coronary artery disease. He had been mentally alert and had never had a stroke. The left carotid sinus was almost occluded by atherosclerosis. In Case 2 there was no history of a stroke, but necropsy revealed an occlusive atheroma of the left carotid sinus and a recent softening of the left anterior putamen and adjacent head of the caudate nucleus. The members of the family were quite certain that he had never had any evidence of a cerebral insult. The patient's mind had remained normal. Case 3 was that of a woman aged 65 who had had no cerebral complaints until the acute onset of extensive myocardial infarction. She was found in a collapsed state, unable to speak, and the jaw so tightly clenched that a drink of tea could not be given. Her eyelids were open, the eyes could be moved, and she seemed conscious. All the limbs were moved, but turning was difficult. The left carotid sinus was entirely occluded by atherosclerosis (Fig. 2), but the brain was normal. The unusual neurological signs may have been determined in part by the fact that one internal carotid artery had been carrying the main blood supply of the entire cerebrum, vascular collapse producing a pseudobulbar type of picture. Two other patients in this group likewise showed no symptoms until a fall of blood pressure occurred, one developing a hemiplegia during the acute stage of cardiac infarction, the other becoming permanently confused during a brief period of shock. In both foci of recent encephalomalacia were seen at autopsy.

*Comment.*—Since the internal carotid artery can in many cases be ligated surgically without immediate cerebral damage resulting, it has been anticipated that atherosclerotic occlusion of the internal carotid artery might often be found unassociated with symptoms. In addition to these seven cases of unilateral occlusion, there may have been a silent occlusion of the first side in three cases of bilateral occlusion. Also, we have examined 13 cases (not included in this study) in which the lumen within the carotid sinus was narrowed to approximately 1 mm., and none of these had had any symptoms definitely attributable to the blockage. However, of the 13 patients, 1 had had a bout of confusion and hallucinations after a small injection of scopolamine, 1 had drunk so heavily that his friends were unable to decide whether he was demented or not, while a third had had several strokes and showed bilateral cerebral lesions thought to be embolic in nature.

In conclusion, total blockage of one carotid artery can exist without symptoms, while a period of abnormal lowering of the blood pressure may unmask a previously silent occlusion. Small cerebral lesions may be associated with the occlusion when a detailed investigation fails to elicit any history of a stroke.

2. *Unilateral Occlusion with Hemiplegia.*—There were 18 cases in this group, and representative examples will be described.

In Case 4 the patient, aged 65, was found struggling to get out of bed one morning, his left side being completely paralyzed. He had had warning attacks of numbness in the left hand, and on five or six occasions had noted transient attacks of complete blindness in the right eye. The blood pressure was 160/90. Recovery was poor, and he died of carcinoma of the rectum three years later. Pathological examination showed complete occlusion of the right carotid sinus by a large plaque of atherosclerosis and a superimposed old thrombus. The vessel above was not remarkable. The brain showed a large, old softening in the frontal region on the right side. Case 5 was that of a man, aged 70, who gradually developed a right hemiplegia and aphasia



Fig. 2 (Case 3).—Cross section of the left carotid sinus and adjacent external carotid artery. The sinus is occluded by a large atherosclerotic plaque.

one week before admission. He had had several focal epileptic seizures in the two previous years, and it was learned that his memory had been failing for about a year. Eight months before his final admission he was found to have left-sided ptosis and miosis. The blood pressure was 170/100. On admission there was severe right hemiparesis associated with aphasia. The patient was slightly confused. Again, the small pupil and ptosis on the left side were noted. The patient died in coma two days later. At necropsy the left carotid sinus was found to be entirely occluded by a large atherosclerotic plaque into which a recent hemorrhage had occurred. Above the sinus the internal carotid artery was distended by a reddish-black clot, which extended distally to the region of the clinoid process (Fig. 3). The territory of the left middle and anterior cerebral arteries was swollen and soft. Case 6 was that of a man aged 62 who lay down for a nap and on awakening found he could not walk or talk. Paralysis gradually increased until the right side was immobile. He had had a headache during the day prior to the onset of the stroke. Examination revealed marked right hemiparesis associated with aphasia. The left pupil was smaller than the right. The blood pressure was 155/80. Recovery was very poor, and the patient died of carcinoma of the rectum 18 months later. On pathological examination the left carotid sinus was entirely occluded by atherosclerosis, and the internal carotid artery distally was reduced to a small solid cord, consisting of a rather normal wall and a yellowish-white core.



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The occlusive process extended to the region of the anterior clinoid process. There was an extensive cavity in the central white matter of the left hemisphere, and the insula had also been destroyed.

*Comment.*—Hemiplegia was the most frequently encountered clinical picture in the present series. Usually the hemiplegia came on slowly in a stuttering fashion over a period of a day or two. It was common for the onset and the periodic worsenings to occur during sleep. Prodromal warnings in the form of fleeting attacks of paralysis, paresthesia, dysphasia, etc., while common, were not nearly so striking as in many of the recorded cases diagnosed by arteriographic means. However, in one case up to six two-minute attacks of numbness of the right hand and right side of the face occurred each day for two weeks before paralysis appeared. It was not unusual for no warning to have occurred at all, at least as far as could be ascertained. Headache above the eye on the side of the occluded vessel has been particularly prominent but need not be present. A partial Horner syndrome

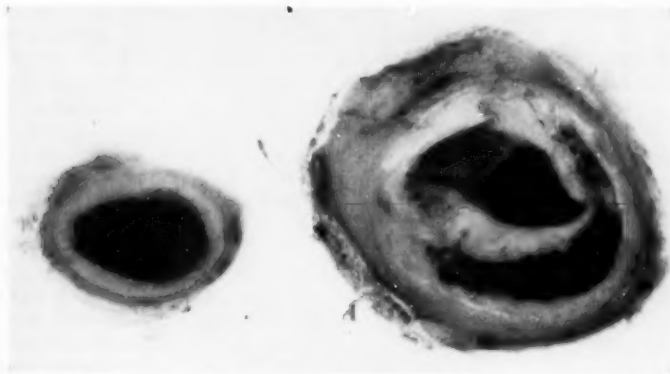


Fig. 3 (Case 5).—Cross sections of the left carotid sinus and of the internal carotid artery 3 cm. distal. The black material is a recent blood clot.

in the form of miosis with or without ptosis occurred in three cases and has been reported in the literature several times. Transient attacks of monocular blindness on the side of the vascular occlusion, fainting spells, convulsions, jerkings of the affected limb, diplopia, and dizziness also occurred. The hemiplegia, which was all too liable to be severe, was usually accompanied by sensory changes, aphasia, or hemianopsia. Of all the clinical findings, the only ones which seemed to be specific and of diagnostic value were transient attacks of monocular blindness, unilateral frontal headache, and miosis in conjunction with contralateral hemiplegia or hemiparesis.

The clinical picture in the present series of cases differs from that described in the literature and diagnosed arteriographically in several particulars. The present group of patients was much older, the cases being scattered evenly from the ages of 60 to 85; the onset in most cases took place over a relatively short period (a day or so), and prodromal warnings in the form of transient attacks of paresis, paresthesia, or speech difficulty were few; a fatal outcome during the acute



phase occurred in 24% of the cases. Furthermore, it was possible in five cases to make a correct diagnosis on purely clinical grounds because of the absence of pulsation in one internal carotid artery.

The pathological findings in the brain in this group of cases consisted oftenest of a softening in the territory of the middle and anterior cerebral arteries. The lesions, in my experience, vary greatly in size and have an atypical distribution not seen in embolic infarcts.

3. *Unilateral Occlusion with Symptoms Arising During Shock or Anoxia.*—There were seven cases in this group, but in only six was the postmortem examination as complete as desired. A few examples will be presented.

Case 7 was that of a man aged 67 who underwent surgical resection of enlarged cervical lymph nodes containing secondary epidermoid carcinoma from the nasopharynx. In the past auricular fibrillation had been noted, but it was not present at the time of the surgical procedure. One hour after operation vascular collapse occurred, and the systolic pressure fell to about 70 mm. Hg. Restorative measures resulted in improvement, but eight hours later it was noted that the patient had left hemiplegia. Coma supervened, and the patient died 72 hours later. The right internal carotid artery within the sinus was almost occluded by an atherosclerotic plaque, and distally the vessel up to its bifurcation into middle and anterior cerebral arteries was distended by a dark clot. Most of the right cerebral hemisphere was softened. Case 8 was that of a man aged 77 who in the past had had no complaints referable to the central nervous system. Twenty-four hours before admission he began to have the pain of myocardial infarction. A few hours before admission, on his being awakened from a nap, he was found to be semicomatose and paralyzed on the left side. On admission the patient was able to carry out only simple commands, and the presence of left hemiplegia was confirmed. The pulse was imperceptible. The patient died two days later, and on pathological examination the right carotid sinus was found to be entirely occluded. There was a recent softening in the right cerebral hemisphere in the territory of the middle cerebral artery.

Case 9 was that of a man aged 75 who was admitted for amputation because of gangrene of the right toes. On the first three postoperative days the patient was restless, confused, and incontinent of urine. On the fourth postoperative day left hemiparesis was noted. He remained paralyzed and confused until his death, 11 weeks later. The patient had auricular fibrillation, and his neurological complication was diagnosed as cerebral embolism. At necropsy the right carotid sinus was observed to be entirely occluded by old thrombotic material, which could have originated as an embolus from the heart. However, there were no other postembolic scars in the brain or other organs. There was an extensive pale infarct of the right cerebral hemisphere in the territory of the middle cerebral artery. In another case of this group the patient went into shock while being tested with an autonomic blocking agent, coma and paralysis being precipitated and death resulting 24 hours later.

Another, more unusual case concerned an elderly woman who complained of a noise in the right side of the head synchronous with the pulse. During the taking of a right-sided arteriogram, which was normal, she blacked out for a few minutes. After a surgical operation, at a later date, she "came out" of the anesthetic with a most severe right hemiplegia, of which she later died. The left internal carotid artery showed an ancient occlusion, and cerebral infarction had occurred on that side during a period of hypotension associated with surgical operation. The right-sided bruit was probably the result of an unusually forceful pulse in the right carotid artery, compensating, so to speak, for the occluded artery on the left. A somewhat similar picture has been seen clinically in another patient, but the head noise was not lateralized.

4. *Unilateral Occlusion Associated with Dementia.*—Eight cases are included here, and five will be presented briefly.

Case 10 was that of a man who during the two years prior to his death, at the age of 72, had become progressively more confused and lethargic. Memory was impaired, and he was subject to episodes of falling. He succumbed to bronchopneumonia. There was severe cerebral

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atherosclerosis, but most striking was virtual occlusion of the left common carotid artery about 2.5 cm. proximal to its bifurcation. In Case 11 the patient, aged 70, had had paralysis agitans for 10 years and, more recently, confusion, hallucinations, and disorientation. The patient died after myocardial infarction, and at necropsy the right carotid sinus was found to be occluded by an atherosclerotic plaque. There were no gross abnormalities of the brain. Case 12 was that

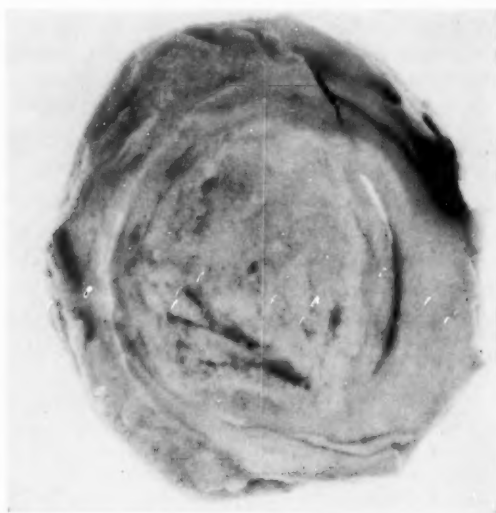


Fig. 4 (Case 12).—Cross section of the left common carotid artery 1 cm. distal to its origin from the aorta. A huge atherosclerotic plaque narrows the lumen to a slit.

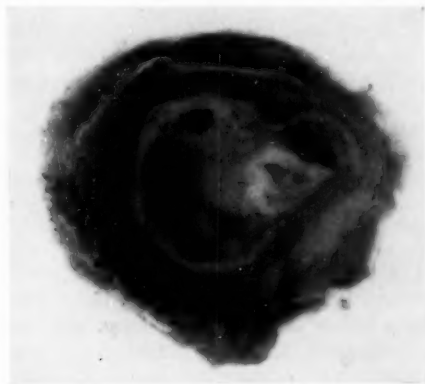


Fig. 5 (Case 14).—Cross section of the left carotid sinus showing complete occlusion of the lumen.

of a woman aged 69 who for a year had shown progressive memory loss, confusion, and irritability. Walking was difficult, and she seemed not to see properly. She died after the onset of a right hemiplegia, and at autopsy the left common carotid artery near its origin from the aorta was seen to be strikingly narrowed by a large atherosclerotic plaque (Fig. 4). The left hemisphere was softened, and an embolus found in the left middle cerebral artery was thought to have arisen distal to the carotid occlusion. In Case 13 the patient, aged 79, had been confused,

disoriented, and hallucinated for about two years before his death. Pathological examination revealed that the left carotid sinus was entirely occluded by an atherosclerotic plaque, and there were no gross lesions of the brain. Case 14 was that of a man aged 77 who had been deteriorating mentally for several months. Without discernible cause, he went into coma during sleep one night and died a few hours later. The only abnormality of the cerebral system was an old, complete occlusion of the left internal carotid artery in the region of the sinus (Fig. 5).

*Comment.*—The association of dementia and carotid occlusion in these cases may be entirely fortuitous, and care must be exercised in drawing conclusions. It is to be recalled that in several instances occlusion or a severe stenosis was found without any sign of mental deterioration. Only further regular examination of the carotid system in cases with and without dementia will allow a final judgment in this matter. This subject will be mentioned again under Group 7.

5. *Bilateral Occlusion with Bilateral Neurological Signs and Coma.*—In this group there were six cases, in four of which there had been a hemiplegia some years previously, presumably due to occlusion in one carotid system. Finally, occlusion of the other side occurred, the patient quickly or slowly lapsing into coma and dying. Two cases will be presented.

Case 15 was that of a man who at the age of 60 had had a transient right hemiplegia and speech difficulty, after which he never regained his former mental acumen. His condition remained the same until 12 years later, when over a period of a few hours he developed a left hemiplegia and became comatose. There was "trismus" of the jaw (Case 3) and a bilateral Babinski sign. Postmortem examination showed the left internal carotid artery to be reduced to a solid cord, while the left common carotid artery was filled with a rust-colored clot. The right internal carotid artery within the sinus showed severe atherosclerosis, and distal to this area the vessel was distended and completely blocked by a recent dark-red clot. There was an old occlusion of the right vertebral artery, and the left was thread-sized. Therefore the brain had received the bulk of its blood supply via the right carotid system, and coma was precipitated when it became occluded.

In Case 16 the patient at the age of 62 developed right hemiplegia, affecting the leg in particular, over a period of some weeks. He told one observer he had had a transitory attack of blurred vision in the left eye. He made a partial recovery, but the leg remained severely paralyzed. His course was uneventful until six years later, when a mild left hemiplegia suddenly appeared and over a period of three days the patient became comatose and died. A Babinski sign was present bilaterally from the onset. At autopsy the left internal carotid artery above the sinus was found to be reduced to a solid cord, while on the right side the sinus was almost occluded by atherosclerosis and the artery distally was distended by a recent dark clot. The brain was softened bilaterally.

*Comment.*—These cases for the most part are straightforward once the underlying vascular pathology is appreciated. The mechanism whereby the first occlusion produced a hemiplegia which remained almost completely stationary for years is not clear. Usually the onset of the original hemiplegia was slowly progressive, indicating a thrombotic process, probably in the internal carotid artery distal to the sinus. At final pathological examination the hemisphere on the side of the final occlusion was more extensively softened than on the other side, which, in addition, bore the scar of the original hemiplegia. While the first occlusion was silent, the final neurological picture closely resembled thrombosis of the basilar artery.

6. *Bilateral Occlusion with Dementia.*—There were five cases in this group, and these will be the subject of another communication at a later date. Here, only a brief summary of each can be given.

## OCCLUSION OF CAROTID ARTERIES

Case 17 was that of a man who died at the age of 67, having become completely demented over a period of five or six years. He finally spent the day sitting in a chair, mute, incontinent, and showing no evidence of mentation. He was found comatose with a right hemiplegia one morning and died two days later. At autopsy both carotid sinuses were found to be narrowed to pinholes by severe atherosclerosis (Fig. 6), and on the left side a clot had formed distally, producing first a hemiplegia, then bilateral neurological signs and coma. The cerebral cortex showed numerous senile plaques. In Case 18 the patient died at the age of 83 after deteriorating mentally for several years. He was confused, disoriented, and with poor memory. There was no pulsation in either internal carotid artery. He died after myocardial infarction, and at necropsy the lumen of each carotid sinus was found reduced to 0.5 mm. or less. In Case 19 the patient, aged 66, had shown loss of memory, apathy, confusion, dysphasia, and helplessness for about a year. Finally he had to be dressed, shaved, and fed. His wife described him as "like a baby." One evening he became more listless, showed flatness of the right side of the face, and died suddenly the next morning. Pathological examination showed occlusive atherosclerosis in both carotid sinuses, no lumen being identified on the left side, while on the right there was only a minute, 0.5 mm. hole.

Case 20 was that of a man aged 57 whose first complaint was difficulty in walking. Over a period of three years he had slowed up markedly and had worked only a few months in that

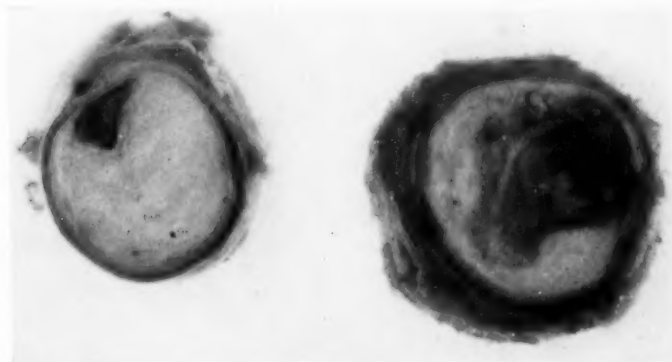


Fig. 6 (Case 17).—Cross sections of right and left carotid sinuses showing the lumens almost obliterated.

period. He would repeat anecdotes and events up to 10 times in one day, forgetting that he had already told them. Yet no severe dementia was described by the family. Three weeks before his death he rather suddenly developed difficulty in swallowing, spoke nonsense, and seemed to lose his mind, following other members of the family around like an infant. Finally he became completely paralyzed, lapsed into coma, and died. At postmortem examination, the left common, external, and internal carotid arteries were found to be reduced to solid cords, the vessel wall surrounding a yellowish-white core. On the right side the region of the carotid sinus was almost occluded by atherosclerosis, while distally a dark-red clot extended upward to the region of the anterior clinoid process (Fig. 7). The right cerebral hemisphere was extensively infarcted; the left less so. On microscopic examination the lumen of the left common carotid artery was seen to be filled with a loose collagenous meshwork, in which small endothelial-lined blood channels lay scattered. A few lymphocytes and macrophages, the latter containing a brownish pigment, were seen, but nowhere did the walls of the vessel show any inflammatory or, indeed, any other abnormal process (Fig. 8).

In Case 21 the patient, aged 81, was admitted because of confusion and difficulty in walking. A detailed history was not obtained. He was disoriented, uncooperative, and refused food. At necropsy he was found to have advanced tuberculosis, but, in addition, both carotid sinuses were reduced to pinholes by large atherosclerotic deposits.

*Comment.*—The importance of bilateral carotid narrowing or occlusion in the pathogenesis of senile dementia remains to be assessed more accurately through continued pathological examination of such cases. It is to be noted that no case of bilateral carotid occlusion without symptoms has yet been encountered. Recently Freyhan, Woodford, and Kety<sup>6</sup> reported an unexplained 25% decrease in the cerebral blood flow in arteriosclerotic dementia and senile psychosis, a finding which especially indicates that carotid obstruction could be of great importance. One of the chief difficulties in judging the importance of carotid occlusion in the

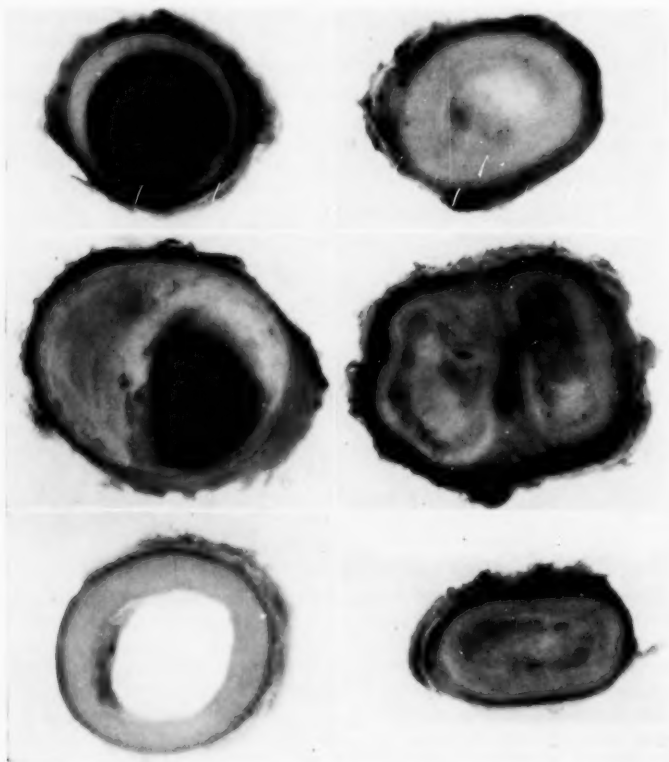


Fig. 7 (Case 20).—Cross sections of each carotid system at three levels, midinternal carotid artery, the region of the sinus, and the midportion of the common carotid artery, respectively, from above down. The right carotid artery is at the left. On the right side, a recent blood clot filled the internal carotid artery and sinus. On the left side, the lumen of the internal and common carotid arteries had been obliterated by an old process.

causation of dementia is the lack of reliable data on the specific gross and microscopic pathological substrate and its localization in the various types of senile deterioration. In the absence of such data one can suspect only that bilateral carotid disease is a cause of the associated dementia rather than a coincidence.

7. *Embolus Arrested at Bifurcation of Common Carotid Artery.*—One of three cases in this group will be briefly outlined.

## OCCLUSION OF CAROTID ARTERIES

Case 22 was that of a man aged 55 who awakened with a severe right hemiplegia and aphasia. At autopsy, 15 days later, a white thrombotic mass, found at the bifurcation of the left common carotid artery, occluded both the internal and the external carotid branches (Fig. 9). There was evidence of other cerebral emboli, as well as infarcts of one kidney. The left cerebral hemisphere was extensively softened.

*Comment.*—Cases such as this illustrate the need to examine the carotid vessels in the neck, especially in unexplained cerebrovascular disease.

8. *Cerebral Embolus Arising from Mural Thrombus Within the Carotid Sinus.*—Four cases were judged to be instances of this phenomenon. Mural thrombus deposited upon atherosclerotic ulceration within the carotid sinus is not infrequent, especially if smaller microscopic deposits are included. Small emboli must often break away without causing symptoms, or even cerebral lesions.



Fig. 8 (Case 20).—Low-power view of left common carotid artery showing the obstruction of the lumen by collagenous connective tissue in which small endothelial-lined blood channels are scattered.

In Case 23 there was a large mural thrombus in the right carotid sinus. The patient had awakened with a severe left hemiplegia, and autopsy revealed extensive softening of the right cerebral hemisphere, attributed to embolism of the middle cerebral artery. No other source for the embolus could be found, and it was tentatively concluded that the embolus arose from the mural thrombus within the carotid sinus.

*Comment.*—It is a difficult matter to conclude with certainty that a cerebral embolus arose from mural thrombus in the carotid sinus. Other sources, such as the lungs, heart, and ascending aorta, must be ruled out by careful examination, and there can be no signs of embolism elsewhere in the body. The diagnosis is therefore made by exclusion. In passing, it might be mentioned that the highly diseased state of the carotid sinus and the fact that embolism from it is possible have led me to test for carotid sinus sensitivity in a gentler fashion than is usually the case.



9. *Cerebral Embolus Arising Distal to Severe Stenosis.*—Five cases seem definitely to fall into this group, but several others were suspected.

The clearest example, Case 24, will be presented. The patient, aged 81, had a left-sided stroke two years previously. She was admitted finally because of a fracture of the neck of the femur following a fall. The hip was pinned, with the patient under anesthesia, after which she remained comatose until she died, five days later. Pathological examination showed an extensive softening of the right cerebral hemisphere and a transtentorial herniation of the temporal lobe. The right carotid sinus was narrowed to a hole 0.5 mm. or less by a large atherosclerotic plaque (Fig. 10). More distally, an embolus (confirmed microscopically) was found tightly occluding the right anterior cerebral artery opposite the mouth of the anterior communicating artery. It was concluded that such a large embolus could not have passed through the remaining lumen of the carotid sinus and therefore must have arisen distally. The embolus probably arrested the blood flow reaching the right hemisphere via the anterior communicating artery.

*Comment.*—The great importance of such an occurrence in explaining the sudden onset of neurological symptoms when the carotid artery is not yet completely

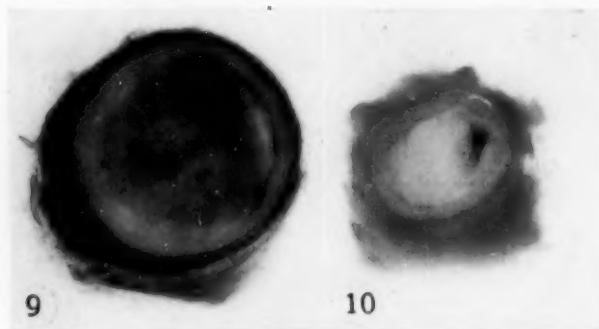


Fig. 9 (Case 22).—Cross section of the left carotid sinus showing an embolic plug lying within. The external carotid artery contained a similar clot.

Fig. 10 (Case 24).—Cross section of the right carotid sinus showing extreme narrowing of its lumen by a large atherosclerotic plaque.

occluded, and, for that matter, even after complete occlusion, has been mentioned earlier in the paper. It has not been possible to get a clear understanding of the manner in which such emboli arise. Slowing of the blood flow, turbulence, or mural deposits are among the possibilities. In one case the embolic material was wholly comprised of platelets. The formation of emboli distal to arterial stenosis or in conjunction with thrombosis is not recognized in other parts of the body (heart and limbs), but it should occur there too.

10. *Miscellaneous Forms.*—Herein are placed (*a*) a case of carotid occlusion associated with vertebral artery occlusion in which a clear-cut clinicopathological correlation could not be made; (*b*) a case of thrombosis of one carotid artery in which coma was later produced by an embolus occluding the vessel of the opposite side, and (*c*) a case showing rather severe narrowing of the lumen in each carotid sinus, yet no history of neurological symptoms or dementia could be obtained. In the third case the patient was an alcoholic derelict.



## COMMENT

Since a brief discussion has been included after each group of cases, further comment need not be lengthy. The discovery of carotid disease with such frequency as is here reported requires a revision of the widespread concept that all cerebrovascular disease is a "cut and dried" subject. It is not widely appreciated that until recently the most careful neuropathological study failed to uncover the nature or pathogenesis of cerebrovascular lesions in at least one-third of the cases. New data on the behavior of cerebral emboli<sup>6</sup> provided the basis for understanding many of these heretofore puzzling lesions, but there remained a substantial residue of unexplained cases. In my experience, routine examination of the cervical portion of the carotid arteries reduces this residuum to less than 5% of cases. Furthermore, carotid occlusion may well explain some cases of senile dementia which previously were not attributed to a cerebrovascular lesion.

The clinical diagnosis of carotid obstruction is often an uncertain one. Carotid arteriography is not justifiable except as part of a research project, so that palpation of the carotid vessels is the only clinical measure available at present. It is my custom first to palpate the common carotid pulsation and, if it is present, to move as high up as possible above the bifurcation, since the block is usually in the internal carotid artery. Various methods of palpation are in use, but I prefer to palpate with the thumbs from in front, i.e., facing the patient, who should be sitting up with the neck slightly extended. The external carotid pulsation can be tested in its temporal branch in front of the ear. When no pulsation whatsoever is felt in the neck, one can make the diagnosis of occlusion confidently if, of course, the patient is not in shock. Conversely, if the pulsation is forceful, the artery is probably quite patent. Comparison of the pulsation with that on the opposite side may be helpful. Yet errors, positive and negative, occur, chiefly because pulsation in the external carotid artery is difficult to distinguish from pulsation in the internal carotid artery. Comparison of the pressure in the central retinal artery on each side by manual methods has not been of help personally, and there is need for a carefully controlled study of such pressures by instrumental means.

Patients with carotid disease are usually over 55, but exceptions occur. As a rule there will be other evidences of atherosclerosis (limbs and heart). Patients with severe hypertension tend not to have significant carotid disease, although, again, there are occasional exceptions. At the time of development of hemiplegia the clinical picture may include fleeting attacks of paresthesia, paresis, blindness, or speech disturbances, as well as headache, dizziness, Horner's syndrome, and fainting spells. Convulsions indicate that a cerebral softening has already occurred.

From a therapeutic point of view no concrete suggestions can be made at this time, but it is anticipated that knowledge of the pathological basis and delineation of the clinical picture, which must always precede logical and orderly advance in therapy, will lead to helpful measures in these cases. Since the pathological substrate of carotid disease is atherosclerosis, the fundamental approach to therapy must be directed at the prevention or cure of that disorder.

SUMMARY AND CONCLUSIONS

Carotid occlusion has been found at routine autopsy in 45 cases in the past two years, its incidence being approximately the same as that of cerebral hemorrhage or hypertensive atherosclerotic encephalomalacia, and about half that of cerebral embolism. Thus, instead of being an uncommon occurrence, carotid occlusion is one of the more frequent disorders.

The pathological picture is complex. The commonest finding is that of atherosclerotic occlusion within the carotid sinus. In addition, there may be recent or old thrombotic occlusion of the internal carotid artery distally. At other times, the atherosclerotic deposit is more proximal, in the common carotid artery. The change in the brain depends on many factors, such as the patency of the opposite carotid artery, the efficacy of the collateral circulation, or the size of the component vessels of the circle of Willis. Occlusion of a carotid artery can take place without demonstrable effect on the brain; it can cause unilateral softening, or it can occasion widespread bilateral changes.

Clinically occlusion may be "silent," but most frequently it leads to hemiplegia. Senile dementia can be associated with unilateral or bilateral occlusion.

Routine examination of the carotid arteries from the arch of the aorta to the clinoid processes provides the solution to many previously puzzling cases of cerebrovascular disease.

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## RECIPROCAL INHIBITION AS THE MAIN BASIS OF PSYCHOTHERAPEUTIC EFFECTS

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THE AIM of this paper is to show that when fundamental psychotherapeutic effects are obtained in neuroses—no matter by what therapist—these effects are nearly always really a consequence of the occurrence of reciprocal inhibition of neurotic anxiety responses, i. e., the complete or partial suppression of the anxiety responses as a consequence of the simultaneous evocation of other responses physiologically antagonistic to anxiety. Several new psychotherapeutic techniques are described that have been derived directly from the reciprocal inhibition principle and have turned out to be of value.

In previous writings \* I presented evidence in support of the view that neurotic behavior is persistent unadaptive learned behavior in which anxiety is almost always prominent and which is acquired in anxiety-generating situations. By "anxiety" is meant the autonomic response pattern or patterns that are characteristically part of the given organism's response to noxious stimulation, and the term is applied irrespective of the duration of the autonomic responses or of what has led to them. An anxiety response is unadaptive when it is evoked in circumstances in which there is objectively no threat.

Successful therapy of experimental neuroses † seems to depend on obtaining reciprocal inhibition of neurotic responses, ‡ for conditioned (learned) inhibition of these responses evidently develops on the basis of their repeated reciprocal inhibition. The mechanisms presumed to be concerned in this process have been discussed in some detail in another connection.<sup>43</sup> Taking a cue from the experimental findings, it was decided to investigate the effects on human neuroses of measures designed specifically to bring about reciprocal inhibition of neurotic responses. Favorable early experiences<sup>41</sup> encouraged the use and further development of these measures, and in 1952 a series of 70 cases was reported,<sup>42</sup> in 86% of which the condition had been either apparently cured or much improved after an average of 25 interviews. A short account of the techniques employed was included in that report. In the present paper these techniques, including new ones, are described in more detail, and the results of treatment of 52 additional cases are set forth.

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\* References 39, 41, and 42.

† References 5, 22, 39, and 42.

‡ References 39 and 42.

EXPERIMENTAL BACKGROUND OF PSYCHOTHERAPY BASED ON THE PRINCIPLE OF  
RECIPROCAL INHIBITION

In the course of experiments during the years 1947 to 1948,<sup>§</sup> I found that cats could be made neurotic merely by placing them in a small cage and then, immediately after presenting an auditory stimulus, subjecting them to a small number of high-voltage, low-amperage shocks from an induction coil. (Previous workers || had mistakenly thought that neurosis would ensue only if the reaction to the shock was in conflict with a previously conditioned food-approach response.) The animals all reacted violently to the shock, showing various combinations of rushing to and fro; clawing at the roof, floor, and sides of the experimental cage; crouching, trembling, howling and spitting, mydriasis, tachypnea, piloerection, and, in some cases, urination or defecation. After a variable number of shocks these reactions would become stabilized, and it would then be found that if the animal was replaced in the experimental cage on a later occasion it would manifest a reaction pattern similar to that observed at the time of the shock. Confinement in the cage for several hours did not diminish the reactions, nor did they show remission when the animals were put in the cage day after day without ever again being shocked. The disturbance was such that an animal starved for 24 to 72 hours would not eat meat dropped in front of him in the cage. Months of absence from the experimental cage did not weaken the reactions evocable there.

It was thus clear that the usual means by which ineffectual responses are eliminated—experimental extinction, which depends upon a process associated with fatigue of the response ¶—was ineffective as far as the anxiety responses were concerned. It seemed for a time as though these responses would have to be regarded as permanent and irreversible, but in our considering possible methods by which they might be eliminated, it seemed reasonable to try causing some other response to occur in the experimental situation that might be expected to be incompatible with the anxiety responses. The obvious response to try was feeding. Neurotic animals were placed inside the experimental cage after having been starved for 48 or 72 hours, and pellets of meat were tossed in front of them. As usual, no eating occurred. Now, since in their living cages the animals were accustomed to having food conveyed to them by the human hand, it was presumed that the hand had become a conditioned food-approach stimulus, and it was hoped that, added to the food-approach tendencies aroused by the sight and smell of the meat, the presentation of the human hand might lead to the overcoming of the inhibition of the feeding response. Accordingly, meat pellets were offered to the animals on an ebony rod held in the hand. Some of the animals ate the food after various periods of hesitation and then took subsequent offerings with increasing readiness.

In those animals that were not induced to eat by the above technique a method was tried that proved to be very instructive. In addition to their reactions in the experimental cage, the animals also reacted with anxiety anywhere in the experimental laboratory and also in each of a series of rooms that had varying degrees of resemblance to the experimental laboratory. They were offered meat pellets in each of these places, starting with the rooms that more closely resembled the laboratory.

§ References 39 and 42.

|| References 1 and 22.

¶ Hull,<sup>11</sup> pp. 277-302, and reference 43.

## RECIPROCAL INHIBITION—PSYCHOTHERAPEUTIC EFFECTS

In the case of each cat a place was eventually found where the evocation of anxiety responses was not great enough to inhibit the feeding response. The animal would be fed about 20 pellets in this place and on the next day would usually be found to accept food in the room next closest in resemblance to the laboratory—as it would not have done previously. From day to day further advances were made, until the animal would eat in the laboratory and eventually, through several stages, in the experimental cage itself. There it would be given numerous pellets of meat on successive days and at last would move about in the cage freely, without any signs of anxiety.

But at this stage the anxiety responses could again be evoked by presenting the auditory stimulus that had preceded the neurosis-producing shocks. The effects of this stimulus could be eliminated in a manner parallel to that applied to the visual stimuli—by feeding the animal first at a considerable distance from the continuously sounding stimulus and then gradually coming nearer day by day. Meanwhile, the auditory stimulus would incidentally have become linked to a food-seeking response; but extinction of this by repeated nonreward did not lead to a recurrence of anxiety in any animal.

These experiments seemed clearly to confirm the expectation of a reciprocal antagonism between the anxiety responses and the feeding responses. As long as, in a given situation, the anxiety was strong enough to inhibit feeding, anxiety would continue to be dominant, and would even increase or spread, as certain supplementary experiments # showed. But if conditions were so changed that the feeding tendency was relatively stronger and feeding could occur in the face of some measure of anxiety, the strength of the tendency to respond by anxiety to the stimuli concerned was gradually weakened.

### RECIPROCAL INHIBITION IN PSYCHOTHERAPY

The above findings led to the framing of the general hypothesis that if a response incompatible with anxiety can be made to occur in the presence of anxiety-evoking stimuli it will weaken the bond between these stimuli and the anxiety responses can be produced in human subjects in a number of different ways. It is not surprising that this should be so, for although Sherringtonian reciprocal inhibition associated with spinal reflex activity is apparently rather specific, at higher levels of organization reciprocal inhibition is clearly often diffuse within the functional "modality" concerned—for example, accompanying the articulation of any word there is ordinarily an automatic inhibition of all simultaneous tendencies to pronounce other words.

The first requirement in a planned attack on neurotic anxieties on the principle of reciprocal inhibition is to determine in what circumstances anxieties are aroused in the patient. Sometimes, usually when the patient has been available for only a small number of interviews, it has been possible to obtain satisfactory results with the therapist knowing only the general character of the situations producing anxiety and without his precisely identifying the disturbing elements. But it is always desirable, and nearly always possible, to examine the situations carefully and to determine in detail to what stimuli the patient reacts with anxiety. To this

# References 39, 41 (p. 615), and 46.

end, it has been found helpful in some cases to make use of the psychogalvanic response (PGR). A careful history of the patient's life and background is, of course, an essential preliminary to the foregoing.

Under the headings that follow it is explained how various responses incompatible with anxiety have their therapeutic effects. Sections 1 to 4 discuss, in the main, techniques that have emerged directly from the reciprocal inhibition principle, and Sections 5 to 8 show how the effects of a number of procedures widely used in the treatment of neuroses are understandable in terms of reciprocal inhibition.

1. *Assertive Responses.*—These responses are mainly employed in situations that occur spontaneously in the normal course of the patient's life. Great prominence has been given to their use by Salter,<sup>20</sup> who, having been led to them by a different theory, seems to apply them almost universally. I have found them of use only for overcoming unadaptive anxieties aroused in the patient by other people during his direct dealings with them. In these circumstances assertive responses are extremely effective. To take a common example, a patient feels hurt when members of his family criticize him and responds by trying to defend himself, by sulking, or by an outburst of petulant rage. Such responses are expressive of anxiety and helplessness. But some measure of resentment is, understandably, almost invariably present at the same time. The patient is unable to express this resentment because, for example, through previous training, the idea of talking back to his elders produces anxiety.

Now, just because this anxiety inhibits the expression of the resentment, it might be expected that if the patient could be motivated to express the resentment, the latter would, in turn, be reciprocally inhibitory to the anxiety and would thus suppress it, to some extent at least. The therapist provides this motivation by pointing out the emptiness of the patient's fears, emphasizing how his fearful patterns of behavior have incapacitated him and placed him at the mercy of others, and informing him that, though expression of resentment may be difficult at first, it becomes progressively easier with practice. It usually does not take long for patients to begin to perform the required behavior, although some need much initial exhortation and repeated promptings. Gradually the patient becomes able to behave assertively in progressively more exacting circumstances and reports a growing feeling of ease in all relevant situations. A conditioned inhibition of the anxiety responses is clearly developing, presumably on the basis of their repeated reciprocal inhibition—a process in all respects parallel to that involved in the overcoming of animal neuroses, as described above. Cases 3, 4, and 5 illustrate this technique.

Obviously, in advising assertive behavior, the therapist must be discreet. He should advise it only when the anxiety evoked in the patient by the other person concerned is unadaptive—in other words, it is an anxiety that occurs even though no unpleasant repercussions can reasonably be expected to follow from making a stand. For nothing can be gained, and sensitivity may even be increased, if the patient's assertiveness should meet with a swift and sharp punishment. For example, however much a person may resent his boss's surly manner, it would in most cases be foolhardy to give frank expression to this resentment. But it is quite frequently possible to express aggression indirectly, through gaining control of an interpersonal relationship by means subtler than overt assertiveness.



Occasionally, when there is unusual difficulty in the expression of aggression in the life situation, it is helpful to initiate the patient by means of a kind of "psycho-drama" in the consulting-room in which the therapist takes the role of some person who in life evokes anxiety in the patient.

2. *Sexual Responses.*—These responses, of course, are mainly of use when anxiety responses have been conditioned to various aspects of sexual situations. When very high degrees of anxiety conditioning have been accompanied by a complete inhibition of sexual responsiveness, other measures, described below, have to be employed. But very often the sexual inhibition is partial and varies according to variations in definable properties of the relevant situations. The patient is told that he must on no account perform sexually unless he has an unmistakable positive desire to do so, for otherwise he may very well consolidate, or even extend, his sexual inhibitions. He is instructed to wait for or to seek out situations in which pleasurable sexual feelings are aroused, and in these he must "let himself go" as freely as possible. If he is able to act according to plan, he experiences a gradual increase in sexual responsiveness to the kind of situation of which he has made use, with varying degrees of generalization to sexual situations of other kinds.

Such favorable consequences occur, it seems, because each time a positive sexual feeling occurs and is intensified by a sexual approach there is reciprocal inhibition of whatever anxieties are also being evoked by the situation, and the strength of the anxiety-evocation tendency is each time slightly weakened. There is no apparent basic difference at all between this process and that which occurred in our cats, in which anxieties were overcome through appropriate manipulations with feeding reactions.

3. *Relaxation Responses.*—(a) *Relaxation Responses in Life Situations:* Jacobson's work has shown<sup>12</sup> that intense muscle relaxation is accompanied by autonomic effects that are antagonistic to the characteristic effects of anxiety. I have repeatedly found clinical confirmation of this in the rapid drop of a pulse rate from 120 to 80 or in the equally rapid drying of profusely sweating palms in a patient who is practiced in relaxation.

Relaxation can be used with lasting good effects in the great majority of cases of neurosis, in my experience. Jacobson himself obtained impressive results by training patients in "progressive relaxation" and then urging them to be as relaxed as possible all the time. It would appear that the improvement in a patient who follows this program may be explained as follows: Persistent relaxation implies some measure of reciprocal inhibition of the effects of any anxiety-producing stimuli that happen to appear, and the occurrence of repeated temporary inhibitions of this kind enables conditioned inhibition of the anxiety responses gradually to develop.

I have sometimes obtained highly gratifying results in patients placed on Jacobson's regime (Case 6), but oftener than not its value is limited, seemingly because the patient is unable to relax at short notice sufficiently deeply to counter the high degree of anxiety produced by the relevant stimulus situations. In a few patients this difficulty has been overcome when the subject has learned how to anticipate such situations and to relax deeply in preparation for them. The following technique, in which the therapist has a good deal of detailed control, has proved to have far wider application.



(b) *Systematic Desensitization Based on Relaxation*: This method of systematic desensitization to anxiety-producing stimuli is carried out in the consulting room.

The patient is given training in progressive relaxation in the course of several interviews. Preliminary experiments on his responses to hypnotic techniques are meanwhile conducted, and during the same interviews steps are taken toward the construction of what is called an "anxiety hierarchy." This is a list of stimuli to which the patient reacts with unadaptive anxiety. The most disturbing items are placed at the top and the least disturbing at the bottom. The arrangement is usually derived solely from the patient's answers to questioning; but occasionally, when he has difficulty in assessing the relative effects of different stimuli, it has been necessary to base the hierarchy, or parts of it, on the psychogalvanic response (PGR). Multiple hierarchies are very often obtained.

In the session after the preliminaries have been completed, the patient is hypnotized and given powerful relaxation suggestions. (A good relaxer can do almost as well without hypnosis, just closing his eyes.) He is then asked to imagine a scene embodying the feeblest member of the anxiety hierarchy. Sometimes it is advisable to start even more mildly, causing the name of the feared object to be visualized. The patient is instructed to signal if at any time he feels more than the slightest disturbance. Usually, two to four items from the hierarchy are presented at each session, the speed of progression depending on how much disturbance is shown or afterward reported. (It is always preferable to advance too slowly rather than too fast. During early experiments with the method I produced serious setbacks in two patients by the premature presentation of stimuli with a high anxiety-evoking potential.) It usually takes between 10 and 30 desensitization sessions before the highest items in the hierarchy can be accepted by the patient without disturbance.

It is natural to ask: Does it follow that because a patient can imagine a scene calmly, he will also be calm when he comes upon a similar scene in reality? Experience shows the answer to be in the affirmative. A very striking example is afforded by Case 7. Sometimes there is a tendency for the real-life improvement to lag behind somewhat, but even then it eventually catches up. The one proviso for success, given the ability to relax, is that the imagined stimulus must at the outset be able to evoke anxiety. A small minority of patients experience no anxiety when they imagine situations that in actuality are anxiety-producing, and in them desensitization is not accomplished by the above procedure. It is interesting to note that recently a patient who repeatedly failed to respond emotionally to images aroused by verbal cues from the therapist has shown considerable disturbance on verbalizing the same situations himself.

The above procedure, originally confined to "simple" phobias, has in the past year been applied to a wide variety of disturbing situations (Case 8), often of a social nature. Sometimes there are multiple distinct, though usually interrelated, hierarchies. These may exist in parallel, or they may be, so to speak, "layered." For example, in a dentist phobic reactions to a variety of work situations were found after a time to depend on fears of criticism, which were, in their turn, partly based on a claustrophobic system. A separate hierarchy was derived from each of these three areas.

4. *Conditioned Avoidance Responses*.—(a) *Conditioned Inhibition of Anxiety Through a Dominating Motor Response*: In 1948 Mowrer and Vick<sup>27</sup> performed

an interesting experiment in which they showed that when rats are repeatedly exposed to a continuous mild electric shock, those animals who are enabled to learn a definite motor response in relation to the termination of the shock develop very little anxiety when placed in the experimental situation minus the shock; and, in contrast to these, much greater anxiety is shown by animals who have no opportunity to learn such a motor response. I have elsewhere<sup>46</sup> given reasons for rejecting Mowrer and Vick's own interpretation of their experiment and have argued that the less anxiety of the first-mentioned group of animals could be attributed to a gradual weakening of the autonomic anxiety responses due to their repeated reciprocal inhibition by the musculoskeletal response that regular reinforcement makes dominant.

It was reasonable to suppose that this experiment might have a therapeutic application. It was postulated that if in the presence of a stimulus evoking neurotic anxiety a mild noxious stimulus were to be applied on repeated occasions, and if this noxious stimulus were at the same time conditioned to produce a well-defined motor response, the neurotic anxiety would gradually be weakened. So far I have found only one case that has lent itself to the use of this method, and in which at the same time the response to other measures was poor enough to warrant the great expenditure of effort and time demanded.

CASE 1.—The patient was a 23-year-old university graduate. She had been unbelievably over-protected during her childhood and adolescence. Three years previously she had had two fairly violent falls in the street within a few weeks and thereafter had been apprehensive of walking outside unaccompanied lest she should fall. As is apt to happen in such cases, her range of activity had then gradually become more and more circumscribed. At one stage she would walk in the street only if her mother held her arm; later she entirely refused to leave the house, and by the time I first saw her, she was practically bedridden, apart from very tense wall-hugging journeys between her bed and a couch in the drawing room. After a year of interviews at approximately weekly intervals, she was feeling more confident and had greatly improved her handling of other people, but was only slightly more freely mobile. Her central fear—of falling—was undiminished, the hypnotic desensitization technique described above having turned out to be inapplicable to her case.

Then the following procedure, based on Mowrer and Vick's experiment, was adopted. Silver electrodes were attached to the patient's left hand and forearm. She was instructed to close her eyes and imagine a relatively easy (though, to her, slightly disturbing) fall and to signal at the commencement of the imagined movement. At this signal a mild electric shock (secondary of inductorium at 8.0 cm. with 6-volt dry cell in primary) was passed into her forearm, being stopped only upon the occurrence of a brisk flexion of the forearm, which the patient had been directed to make. This movement soon became the instant response to the shock. When the whole sequence had been repeated a number of times, the patient reported that imagining the fall was becoming less unpleasant and disturbing, and, after further repetitions, that she could imagine it with ease. Thereafter, she was able to attempt this particular fall in actuality, and after practicing it a good many times a day, she could do it easily after a few days. Then she was ready for a slightly more difficult fall. Standing at increasing distances from chairs and other supports was later accomplished in similar fashion. The procedure was repeated at intervals of approximately five days, and as she became capable of falling farther and harder and, later, of standing farther from a support, she was able to walk and move around with increasing freedom. (It is intended to publish separately a detailed account of this case.)

(b) Conditioning of "Anxiety-Relief" Responses: The possibility that "anxiety-relief" responses might be directly conditioned to convenient stimuli and subsequently used to counter anxiety was suggested by an observation in a recent experiment by Zbrozyna.<sup>47</sup> This observation was that if a stimulus is repeatedly presented to an eating animal just before withdrawing the food, that stimulus

acquires the property of inhibiting feeding even when the animal is in the middle of a meal. By analogy with this, it seemed reasonable to expect that if an uncomfortable induction shock were administered to a human subject for several seconds and were then made to cease immediately after a signal, that signal would become connected to such bodily responses as would follow cessation of the shock, and, furthermore, that these responses would be the negative of the anxiety that had been produced by the shock. This, it was hoped, would imply the acquisition of an additional means of inhibiting anxiety due to other stimuli.

This idea has been put into practice in eight patients, with results according to expectation in all but two. With the inductorium set at about 7.5 cm. (but varying according to the subject's reaction) and a primary inflow of 6 volts, a continuous shock is administered to the subject's left forearm. He is told to bear it until the desire to have it removed becomes very strong, then to say aloud the word "calm." As soon as he says the word, the current is switched off. This is repeated 10 to 20 times in a session. Most subjects report a feeling of relief at the cessation of shock that seems profoundly out of proportion to the disturbing effect of the shock and find, after one to three sessions, that using the word in disturbing situations decreases the disturbed feeling. In one case the word "calm" did not become the effective conditioned stimulus to the relief reaction, but the subject reported that she found herself automatically picturing the inductorium against the background of the consulting room whenever she experienced anxiety rising within her. This would bring on "surges of relief," under which the anxiety would melt away. Gradually, according to prediction on the reciprocal inhibition principle, with repeated occurrences of this experience the amount of anxiety produced by the relevant stimuli became less and less. (It should be noted that this technique has in no case been the sole method of treatment.)

(c) Avoidance Conditioning of Obsessions: In the production of reactions of avoidance to obsessional stimuli, we have an instance of the application of the reciprocal inhibition principle to a response other than anxiety, for here it is an intense and excessive approach response that is being overcome. The essence of the method is to subject the patient to a very unpleasant electric shock in the presence of the obsessional object. It seems that the first to report the use of such a method was Kantorovich,<sup>16</sup> who employed it in the treatment of alcoholics—with considerable success. The technique was first applied to an obsessional patient by Max<sup>23</sup> a good many years ago and was then apparently ignored. Max administered to his patient an unusually severe induction shock in the presence of a fetishistic object. By doing this repeatedly and then reinforcing at intervals when required, he produced a persistent avoidance reaction to this object, which alone, it seems, very greatly ameliorated the patient's emotionally disturbed state.

CASE 2.—I have used a modification of Max's method in the treatment of a food obsession of 16 years' standing, which previously had completely resisted almost every current mode of therapy, from ECT to psychoanalysis. The patient was a very intelligent woman of 36 who had long suffered from cardiac insufficiency and was on a restricted diet. Besides the obsession, she had other exceptionally severe and distressing neurotic reactions, which had improved considerably on the more usual reciprocal inhibition techniques. But the obsession was still present almost always and was worse when the patient was reacting to any persistent anxiety-producing stimulus. She would have visions of various items of delectable food and would be tortured by a conflict as to whether to eat or not. If she did eat, she soon felt a rising guilt (anxiety about

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something done) which would lead back to the obsession. Thus, a vicious circle of eating and anxiety would be started, which, within a few days, would leave her in a desperately helpless and exhausted state.

Avoidance conditioning was carried out as follows: The electrodes having been attached to her left forearm, the patient was told to raise her right hand as soon as she had formed a clear imaginary picture of some desirable foodstuff. An almost unbearable current from the inductorium at 7.0 cm. (6 volts) was then instantly delivered and continued until she lowered her right hand as a signal that the shock could no longer be borne, as she usually did after a second or two. About 10 reinforcements were given at each session, and two to three days were allowed to elapse between sessions. After the first session the "nagging" of the obsession was already markedly reduced. It was further reduced in four more sessions, which implicated the whole range of items of "delectable food." The patient reported that on imagining any such food she immediately had a feeling of fear and revulsion, accompanied by an image of the shock situation. (At an earlier stage this feeling was occasionally preceded by a momentary feeling of pleasure.) Within a few seconds she was able to return her attention to whatever she had been doing before the food image came up—a tremendous gain as contrasted with the old misery of hours spent debating, "Should I eat; should I not?" After her fifth, and last, session she stated that her tendency to think of food was also diminishing. Unfortunately, but not unexpectedly, there was also some generalization of the avoidance to permitted foods, i. e., nonfattening sodium-free foods eaten only at mealtime. This was a very considerable difficulty, but the patient regarded it as trivial in comparison with her obsession. The over-all lightening of the burden made it much easier to return to the usual procedures for overcoming the anxiety reactions. Gratifying progress was made, only to be brought to an end by the patient's sudden death from ventricular fibrillation due to chronic rheumatic heart disease.

5. *Feeding Responses.*—I have not employed feeding responses to obtain reciprocal inhibition of anxiety in human subjects, but Jones<sup>14</sup> has done so successfully in young children. There is no reason why feeding should not be effective in overcoming fears in adults under certain circumstances. What is required is that in the presence of the anxiety-evoking stimulus food must be given under so intense a hunger drive that in the act of eating there will be an inhibition of anxiety. Probably, it is precisely this that is the explanation of the beneficial effects on neuroses of subcoma doses of insulin\*; and it is worth noting that the effects of this method have been greatest when the patient has eaten substantially more than usual and has put on weight. Presumably, in eating voraciously because of heightened hunger drive, the patient obtains a reciprocal inhibition of any anxiety responses that happen to be occurring within him at that particular time. This explanation, with its close parallel in animal experiments, gains credence when one takes into account the haziness of the explanations that have been offered in terms of gross physiology. However, from the results of a controlled experiment by Teitelbaum and associates,<sup>34</sup> as reviewed by Sargant and Slater,<sup>35</sup> it is clear that only a small percentage of patients are favorably affected by subcoma insulin. This finding is not surprising, because any effects depend on the fortuitous occurrence of anxiety-producing stimuli at the time of the eating (this implies, of course, that the patients who should respond best are those that have a good deal of so-called free-floating anxiety, i. e., secondary conditionings of anxiety to commonplace stimuli, such as room walls or voices).

6. *Respiratory Responses.*—In 1947 Meduna<sup>24</sup> reported the very interesting discovery that in many patients neurotic reactions can be ameliorated, and some-

\* References 21 and 32.

times even overcome, by inhalations of high concentrations of carbon dioxide. His usual technique has been to make the patient breathe a mixture of 30% carbon dioxide and 70% oxygen until consciousness is lost. More recently, La Verne<sup>19</sup> has claimed equally good or better results from single full-capacity inhalations of 70% carbon dioxide and 30% oxygen, usually producing no more than stupor. Meduna and his followers have assumed that the effects of this kind of treatment are due to the depressing action of carbon dioxide on nerve structures. Gellhorn<sup>†</sup> has criticized Meduna's theory and has gone on to suggest another explanation of these effects, also in terms of gross physiology. But from a psychological point of view any such theory is untenable, because the treatment apparently affects only neurotic anxiety responses. If the effects of carbon dioxide were due to its action on some chemical factor in certain nerve cells, all cells containing this factor would be influenced; and since the relevant cells are those that in one way or another subserve anxiety responses, all anxieties, even those aroused in response to real threats, would be similarly diminished by the treatment. Neither Meduna's case histories nor my own personal experience reveals any indication of this happening. Anxiety responses, as such, are by no means removed from the repertoire of the patient, who continues to have and display normal anxieties. It is therefore to be concluded that a specific unlearning of the connection between certain stimuli and the anxiety responses has occurred.<sup>43</sup> It is reasonable to suspect that the unlearning occurs by a process of reciprocal inhibition in this instance, too. Neurotic anxiety-producing stimuli are brought forth during the dreamy or confused stage of the treatment, or are already present if there is "free-floating" anxiety. Processes antagonistic to anxiety can be found both in the excitation that goes with intense respiratory stimulation and in association with the complete muscle relaxation that high concentrations of carbon dioxide produce.<sup>‡</sup>

I have occasionally treated patients with carbon dioxide, employing La Verne's method because, in contrast to Meduna's, it arouses little or no anxiety. Of five patients, one was completely unaffected, two felt sedated afterward for the rest of each treatment day, one showed slight but definite lasting improvement, and one obtained very marked benefit. The last-mentioned had a war neurosis of 10 years' standing. He displayed, almost continuously, a high degree of "free-floating" anxiety and had a special sensitivity to all situations involving explosions or low-pitched rumblings. Desensitization under hypnosis could not even be started because when asked to imagine a scene the patient could never visualize anything but irregular black and white blotches. He had three treatments, each consisting of two full inhalations of the mixture of 70% carbon dioxide and 30% oxygen. There was a week between treatments, and he felt persistently better after each. After the third treatment he said he felt perfectly well. Three months later he was still well and reported that thunderstorms had left him quite undisturbed, in contrast with the past.

*7. Interview-Induced Emotional Responses.*—Cures of neuroses seem to be obtained by all kinds of therapists, even though, owing to their different theories, they devote the interview period to procedures that differ in a large variety of

<sup>†</sup> Gellhorn,<sup>7</sup> p. 462.

<sup>‡</sup> Gellhorn,<sup>7</sup> p. 459.



ways. Such studies as have compared the success of various kinds of interviews have shown no important differences either in the percentage of cures or in their quality. § Wilder,<sup>35</sup> for example, found that the psychotherapeutic results achieved by hospitals, mental hygiene clinics, psychoanalytic institutes, private psychoanalysts, and private psychotherapists were much the same. This finding strongly suggests that the various special points of procedure that the different therapists regarded as crucial to success were not crucial at all, and that the effective factor must have been something that all the therapeutic situations generated in common.

The only feature common to all the therapies seems to be that there is a private interview in which the patient confidentially reveals and talks about his difficulties to a person he believes to have the knowledge, skill, and desire to help him. This kind of situation undoubtedly excites emotional responses in patients, and both the character and the strength of these responses vary as functions of many factors, of which the personality and attitude of the therapist and the individual reactive potentialities of the patient are presumably the most important. If, in a patient, the emotional response evoked by the interview situation is (a) antagonistic to anxiety and (b) of sufficient strength, it may be supposed that it will reciprocally inhibit the anxiety responses that are almost certain to be evoked by some of the subject matter of the interview.

This hypothesis requires systematic testing, but it is my clinical impression that those patients who display strong emotions other than anxiety during the early anamnestic interviews are the ones who are likely to show improvement before special methods for obtaining reciprocal inhibition of anxiety responses are applied.

8. *Abreaction*.—Abreaction may be defined as the emotional reevocation of a fearful past experience. It is a special case of the interview-induced emotional reactions considered under the previous heading. It may occur under thiopental (Pentothal), hypnosis, or deep relaxation, or even in the course of an ordinary interview. The emotion is of considerable intensity, and beneficial effects seem, by and large, to be positively correlated with its intensity. But, as Grinker and Spiegel<sup>||</sup> have pointed out, if unrelieved terror is the only emotional component of the abreaction, the patient makes no progress. It is only when the patient can feel the impact of the therapeutic situation, e. g., the therapist's sympathetic acceptance of him, that beneficial abreaction can occur. This is emphasized by Grinker and Spiegel's observation ¶ that "abreactions that occur spontaneously under alcohol are nontherapeutic." In the case of abreaction, too, then, benefit depends on the evocation of other emotional responses in association with the fearful situation, so that, presumably, reciprocal inhibition of anxiety occurs. The specially dramatic changes sometimes produced by abreaction are in line with the experimental finding that modifications of response are likely to be more marked when there is a higher level of drive to be reduced. #

If the above interpretation is correct, it would follow that the uprooting of "repressed memories" is not essential to the therapeutic effects of abreaction, although the ventilation of forgotten material often provides the subject matter.

§ References 18 and 35.

|| Grinker and Spiegel,<sup>9</sup> p. 81.

¶ Grinker and Spiegel,<sup>8</sup> p. 392.

# References 11 and 40.

Many of Grinker and Spiegel's patients\* were improved by abreactions in which the battle experiences concerned were well-remembered ones. The case that follows demonstrates how irrelevant to a patient's recovery the restoration of forgotten memories can be.

CASE 3.—A 37-year-old miner was seen in a state of intense anxiety. He had had a very marked tremor and total amnesia for the previous four days. He gave a story that his wife, on whom he was greatly dependent, had cunningly got him to agree to "temporary divorce" six months before and was now going to marry a friend of his. No attempt was made at this juncture to recall the lost memories. The patient was made to realize how ineffectual his previous attitudes had been and how he had been deceived. As a result, he angrily "had it out" with his wife (and a few others, incidentally); anxiety rapidly decreased, and he soon felt strongly motivated to organize his whole life differently. At his fifth interview (10 days after treatment began), he said that he felt "a hundred per cent," and looked it, and he was full of plans for the future. Yet, he had still recalled nothing whatever of the forgotten four days.

Since the possible effects of restoring the memories at this stage were obviously a matter of great interest, the patient was then deeply hypnotized and told to recount the story of the four days. He narrated in detail how he had traveled 300 miles to his rival, meaning to strangle him; how he had been fobbed off, and how, returning, and at last hearing from his wife's own lips that she was in love with the rival, he had staggered out of the house, made his way to his sister's

TABLE 1.—Classification of Cases

Category	Number		
	1952 Series	Present Series	Total
Anxiety states .....	39	33	72
Hysteria .....	6	3	9
Reactive depression .....	7	3	10
Obsessions and compulsions .....	5	6	11
Neurasthenia .....	3	0	3
Mixed and unclassifiable .....	10	7	17
Totals .....	70	52	122

house, and there collapsed. He told all this quietly, with little emotion, except where he described meeting his rival. Then he moved his hands as if about to throttle someone. He was given the posthypnotic suggestion that he would remember the whole story on waking. When he woke, he told it again briefly, expressing slight amusement at it and surprise at having remembered. There were no important consequences. A few months later he married another woman and was apparently very well adjusted generally. After four years there has been no evidence of relapse.

## RESULTS

In 1952 the results were reported of the treatment of 70 patients by the reciprocal inhibition techniques that were then available.<sup>44</sup> In the 52 additional cases now presented, these were the techniques that were again chiefly employed; but, in addition, the three induction coil methods described above and La Verne's method of carbon dioxide therapy were occasionally used.

Both series include only patients whose treatment has ceased after they have been afforded a reasonable opportunity for the application of the available methods; i. e., they have had as a minimum both a course of instruction on the changing of behavior in the life situation and a proper initiation of a course of relaxation-desensitization. This minimum takes up to about 15 interviews, including the anamnestic interviews, and no patient who has had 15 or more interviews has been omitted from the series. Almost invariably, when a patient has experienced

\* Grinker and Spiegel,<sup>9</sup> pp. 83-84.



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some early improvement, he continues until improvement is very marked, and then, oftener than not, breaks off treatment, even though I am not quite ready to discharge him.

The degree of response to treatment has been estimated by reference to Knight's five criteria<sup>17</sup>—symptomatic improvement, increased productiveness, improved adjustment and pleasure in sex, improved interpersonal relationships, and ability to handle ordinary psychological conflicts and reasonable reality stresses. In addition, the patient's score on Willoughby's questionnaire † is compared with his score at the beginning of treatment, and no patient is regarded as greatly

TABLE 2.—Results of Reciprocal Inhibition-Based Psychotherapy

	No. of Cases	Apparently Cured	Much Improved	Slightly to Moderately Improved	Unimproved
1952 series .....	70	34	26	7	3
Present series .....	52	20	20	1	1
Totals.....	122	54 (44%)	56 (46%)	8 (7%)	4 (3%)

TABLE 3.—Distribution of Interviews

No. of interviews.....	Up to 10	11-20	21-30	31-40	Over 40	Total
No. of patients.....	12	17	12	3	8	52
Mean number of interviews per patient 26.1						

TABLE 4.—Comparative Results

Series	No. of Cases	Apparently Cured or Much Improved	Improvement Moderate, Slight, or Nil
Berlin Psychoanalytic Institute <sup>17</sup> .....	263-402*	163* (62-40.5%)	100-239* (38-59.5%)
New York Hospital <sup>18</sup> .....	100	53 (53%)	47 (47%)
Combined reciprocal inhibition series.....	122	110 (90%)	12 (10%)

\* See text.

benefited unless his score has dropped markedly, preferably to 20 or less. On the basis of these criteria, results are grouped under the headings used by Knight: (1) apparently cured; (2) much improved; (3) moderately to slightly improved; and (4) unimproved.

In Table 1 the cases are grouped according to the "type" of neurosis. This grouping has little value from any clinical angle, for almost all neuroses are really "mixed," and the compartment into which a case falls is no guide to its tractability.

Table 2 shows the results of reciprocal inhibition-based psychotherapy in our two series. It will be noticed that in the present series the percentage of good results has risen slightly, but a more rigorous standard has been applied for

† References 36 and 37.

"cure." Systematic long-term follow-up studies have not been done, but information has been received from 14 patients of the 1952 series. Not one of these has relapsed, and all but one have reported continuing progress two to five years after the end of therapy.

Table 3 subdivides the present 52 cases according to the number of interviews given. Four-fifths of the patients had 30 interviews or less. The mean is 26.1, as compared with a mean of 24.9 in the earlier series. It may be noted that in the two series there was a total of 13 patients who had previously been psychoanalyzed, and these had an average of 51.7 interviews. Part of the reason for this high average was that some of these patients were exceedingly verbose and found difficulty in participating in treatment by objective techniques. Nevertheless, 10 of the 13 patients were either apparently cured or much improved. It is interesting to note that two psychoanalyzed patients, while repeatedly expressing skepticism regarding the present methods during their early interviews, nevertheless agreed to follow out instructions, and both did very well—one being apparently cured after 14 interviews and the other much improved after 16. Another such skeptic, however, was the only patient in the present series who made no improvement at all.

Table 4 compares the total results of our two series with those of Hamilton and Wall's New York Hospital series<sup>10</sup> and those of the largest reported psychoanalytically treated series<sup>17</sup>—from the Berlin Psychoanalytic Institute. In the case of the last series, two figures are given for both the total number of cases and the percentages. The larger total includes those patients who had less than six months' psychoanalysis. But for the purposes of our comparison the smaller, and more favorable, total is taken. The  $\chi^2$  test for significance yields a value of 44 when our results are compared with those of the New York Hospital series, and a value of 31 when they are compared with those of the psychoanalytic series. Thus, both comparisons indicate that the probability that the higher proportion of successes in the present series is due to chance is negligible.

The crucial point of the comparative figures in Table 4 is that 90% of the patients in our two series were either apparently cured or much improved, and only about 60% of the cases in the other two series. If the favorable results of the present series are, to the extent of 60%, regarded as due to the nonspecific reciprocal inhibition that would occur in any kind of interview situation, the additional 30% of good results appears to be attributable to the special measures for obtaining reciprocal inhibition described above. Furthermore, the small average number of interviews needed suggests that the use of these special measures early in treatment greatly accelerates the improvement of those patients who would have responded to the nonspecific factors alone.

#### COMMENTS ON OTHER THEORIES OF THE PSYCHOTHERAPEUTIC PROCESS

In reciprocal inhibition we have a single principle that can explain (a) the effectiveness of measures used to overcome animal neuroses, (b) the similar success of various, often widely different, interview techniques, and (c) the effectiveness of certain special measures—subcoma insulin and carbon dioxide therapy. At the same time, the principle has led directly to the development of effective new psychotherapeutic techniques, as described above.

It is necessary at this point to examine some other current theories to see whether any of them can, with equal ease, cover the same range of facts. The theories will not be considered in relation to all the facts. If any theory is found to contradict even one major fact, that finding is sufficient to challenge the validity of that theory. It will be seen in what follows that on this basis there is cause to reject each of the more or less influential theories considered.

1. *Psychoanalytic Types of Theory*.—(a) Pure Psychoanalytic Theory: The essential features of this type of theory have been described in great detail by Fenichel.<sup>6</sup> Neurotic symptoms are regarded as due to "distorted discharges" that come from the damming up of the energies of repressed memories, and the essential aim of psychoanalytic psychotherapy is to remove the repressions and so let the memories be reintegrated into the patient's conscious life. In Fenichel's words,‡ "The therapeutic task, then, is to reunite with the conscious ego the contents (both unconscious anxieties of the ego and instinctual impulses of the id) which have been withheld from consciousness by counter-cathexis." Now, the accomplishment of this "therapeutic task" cannot really be the essence of psychotherapy, because other methods which do nothing to lift repressions produce individual cures as impressive as any that psychoanalysis can claim, as often and at least as rapidly (in the present series apparently oftener and certainly more rapidly). Fenichel § is well aware that methods other than psychoanalysis have psychotherapeutic effects; but, on the basis of his theoretical presuppositions, and without empirical support, he discards these effects as being limited in comparison with those of psychoanalysis. Meanwhile, the findings of Landis<sup>18</sup> and Wilder,<sup>25</sup> mentioned above, are contrary to Fenichel's presumption, as are the results of the treatment recorded here, with its high proportion of cases fully satisfying all of Knight's criteria.

Unfortunately, there is little likelihood that psychoanalysts in general will take the above considerations into account, any more than they have in the past taken account of facts or arguments unfavorable to their theories. It is not easy even for a strict scientist to give up a favorite hypothesis when the evidence fails to support it; but psychoanalysts seem especially liable to acquire habits of thought that do not conform to the requirements of science, as Ellis' recent monograph clearly shows.<sup>3</sup> Perhaps it is this that explains why such serious criticisms of the psychoanalytic position as those of Wohlgemuth,<sup>28</sup> Johnson,<sup>13</sup> Salter,<sup>21</sup> and Eysenck<sup>4</sup> are glossed over or ignored.

(b) A Behavioristic Translation of a Psychoanalytic Theory of Psychotherapy: In an interesting book, Dollard and Miller<sup>2</sup> have tried to interpret the psychotherapeutic process in terms of the Hullian theory of learning.|| They accept as fact the psychoanalytic account of what happens. For instance, they say,¶ "The patient is sick just because his mind is lamed by repression, and he cannot use it freely to solve his problems," and imply # that in a severe neurosis a therapist who is not concerned to remove repressions is unlikely to achieve "a complete cure." We have seen above that in view of the failure of psychoanalysis to

‡ Fenichel,<sup>6</sup> p. 570.

§ Fenichel,<sup>6</sup> p. 555.

|| References 11 and 26.

¶ Dollard and Miller,<sup>2</sup> p. 301.

# Dollard and Miller,<sup>2</sup> p. 322.

obtain superior results there is no justification for this opinion. It is interesting, also, to note that, although the book is largely built around an account of a successfully treated case, that of Mrs. A, there is no point at which Mrs. A can clearly be seen to be benefiting from the lifting of repressions in the sense defined by the authors.

However, leaving repression aside, Dollard and Miller have given a very detailed and absorbing account of many of the occurrences that may be observed during psychotherapy. But on the matter of interpretation one must again quarrel with them. They regard extinction, i. e., conditioned inhibition based on reactive inhibition,\* as the main mechanism subserving elimination of neurotic habits.† Now, while it cannot be denied that fear can undergo extinction, this process is usually very long and difficult, as Dollard and Miller themselves remark.‡ For example, Miller found<sup>25</sup> that a fear-motivated motor habit required hundreds of trials to be extinguished. Thus, when fear responses are eliminated rather rapidly, either experimentally or clinically, it must be presumed that some mechanism other than extinction is at work—and reasons are given above for believing that reciprocal inhibition is the basis of this mechanism. Dollard and Miller do actually give consideration to the therapeutic effects of responses incompatible with neurotic responses,§ but apparently regard these effects as having only minor importance. Yet, in most of the therapeutically effective events they describe in the case of Mrs. A it is possible to see how the anxiety is inhibited by antagonistic emotions arising either directly from the therapeutic relationship or as a consequence of the therapist's intervention. The following is an example: At a certain stage || the therapist points out to Mrs. A that now that she is an adult she will not be punished if she acts independently. Dollard and Miller state that this suggestion had two important effects—to inhibit fear of taking necessary actions and to create hope of a way out. But the mere realization that she would not be punished could not be expected to have much fear-inhibiting effect. Patients are very often fully aware that their fears are unreasonable and yet go on having them. What the therapist really seems to have done is to motivate Mrs. A to take action, and it is the taking of this action which is "anti-anxiety" in effect and of far more potency in diminishing anxieties than talking or "realizing" could ever be.

2. *Conditioned Reflex Theories.*—(a) Pavlovian Theory: Pavlov's theory of psychotherapeutic effects follows directly from his theory of the basis of neurosis. According to Pavlov, normal cortical function requires a balance between excitatory and inhibitory processes. If at a given locus of the cortex excitation and inhibition come into conflict with each other at high intensity, the neural elements concerned may be unable to bear the strain and so undergo a pathological change by which the balance is overthrown; and then the animal presents neurotic symptoms.¶ In accordance with this hypothesis, the essence of therapy would be to restore the balance, as Pavlov essayed to do by administering bromides, with

\* Hull,<sup>11</sup> pp. 277-287, and reference 43.

† Dollard and Miller,<sup>2</sup> pp. 230-232.

‡ Dollard and Miller,<sup>2</sup> pp. 71-73.

§ Dollard and Miller,<sup>2</sup> pp. 74, 383-387.

|| Dollard and Miller,<sup>2</sup> p. 316.

¶ Pavlov,<sup>28</sup> pp. 292-293.

the idea of strengthening the inhibitory process, and in many cases he succeeded in curing the neurosis. He later obtained better results from a combination of bromides and caffeine.<sup>#</sup> It has been shown elsewhere<sup>30</sup> that the curative effect of bromides could be due to the fact that they have a selectively greater depressing action on anxiety responses, favoring their reciprocal inhibition by any antagonistic responses that happen to occur. Pavlov's theory, on the other hand, would be hard put to it to explain how *lesions* in the nervous system could be healed either by a drug that depresses nervous activity or by retraining procedures that involve nothing more than the formation or undoing of specific neural connections.

(b) *Salter's Excitation Theory*: Salter<sup>30</sup> has recently offered a theory of psychotherapy which is broadly based on Pavlovian psychology but which apparently derives its special form from the clinical experience that if neurotic patients are encouraged to express their habitually inhibited nonanxious feelings, they often gradually overcome their neuroses. He holds that a person with a neurosis suffers from an excess of inhibition, and it is therefore through the arousal of excitation that this expression of feelings overcomes a neurosis. For Salter, it is on the basis of excitation alone that a neurosis can be cured.

There are several reasons for rejecting this theory. It may be noted that Pavlov himself did not regard an animal as neurotic just because its temperament was a highly inhibitory one but found that both excitatory and inhibitory animals could develop neuroses. The following criticisms are more directly relevant: First, even though it is true that in association with the anxiety many other responses are inhibited, the anxiety responses themselves, especially clearly in acute anxiety states, are quite evidently excitatory. Second, relaxation techniques, involving a negation of excitation, are, as described above, very effective in the treatment of neuroses. Third, electroconvulsive therapy, whose effects on the nervous system are eminently excitatory,\* is not of great value in treating neuroses, with the exception of some depressions.<sup>15</sup> Even the most favorable series<sup>20</sup> give no better results than would be obtained from nonspecific interview-induced psychotherapeutic effects, and such effects would doubtless occur even when shock therapy is what the therapist is using.

#### FURTHER CASES ILLUSTRATING PSYCHOTHERAPY BASED ON RECIPROCAL INHIBITION

CASE 4.—A married woman of 24 was first seen on April 14, 1951, complaining of chronic anxiety and a feeling of inadequacy in most of her social relationships, of which the most distressing was that with her mother-in-law. She had special phobic reactions to certain men, which turned out to depend on the degree of their resemblance to her father, and she also reacted with fear to the ringing of the front doorbell or the sound of footsteps up the garden path. All these reactions were tied up with the early behavior of her father, who was extremely sadistic and had terrorized her in her childhood in a great variety of ways. When she was 14, he removed her from school to work in one of his shops without pay. He would frequently creep up silently and pounce on her for not working hard enough. At 17 she ran away to Johannesburg from her family in Cape Town, and at 21 married a motor mechanic, with whom she was generally happy.

The patient had 65 therapeutic interviews, unevenly distributed over 27 months. The greater part of the time was devoted to discussions of how to gain control of her interpersonal relationships and stand up for herself. She had considerable difficulty with this at first, even though it

# Pavlov,<sup>20</sup> pp. 95-97 and 181.

\* Gellhorn,<sup>7</sup> pp. 438-442.

had early become emotionally important to her to please the therapist. But she gradually mastered the assertive behavior required of her, overcame her anxieties, and became exceedingly self-reliant in all interpersonal dealings, including those with her mother-in-law. Finally, she deliberately made a trip to Cape Town to pit herself against her father. She experienced initial nervousness at their first meeting but after that was in complete control, during a three weeks' stay.

At the conclusion of therapy, in June, 1953, she was adjudged a very well-adjusted and competent person and early in 1954 reported that she was still going from strength to strength.

**CASE 5.**—An attractive woman of 28 came for treatment because she was in acute distress as a result of her lover's casual treatment of her. Every one of very numerous love affairs had followed a similar pattern—first she would attract the man, then she would offer herself on a platter, crawling and cringing and leaning on him heavily. He would soon treat her with contempt and after a time leave her.

In general she lacked assurance, was very dependent, and was practically never free from feelings of tension and anxiety. Her Willoughby score was 45, reflecting very considerable neuroticism. A year previously she had terminated a two-year course of psychoanalysis, which had benefited her somewhat. She came to me only because her analyst was not available, and during the first few interviews she repeatedly expressed doubt regarding the value of my non-analytic treatment.

At her fifth interview the unadaptiveness of her anxieties and the rationale of the reciprocal inhibition principle were explained to her, and she left feeling optimistic. At the next interview she was told how to behave with firmness and take independent courses of action with her lover. This involved a good deal of subtle tactics. She performed well according to prescription and was able to terminate her relationship with him with dignity and with relatively little disturbance, and, indeed, with a certain feeling of triumph. Meanwhile, she was shown how to counterattack her nagging mother and to deal with her boss and other people who easily upset her. Through action she gradually developed a feeling of mastery, both at home and at work.

Soon she found that she was beginning to hold the reins in a variety of minor sexual situations. After her 13th interview, she went on a holiday and returned six weeks later to say that she had made continued efforts to control interpersonal situations and was feeling much more stable emotionally. She was much better poised and had been a social success for the first time in her life. She no longer felt, as in the past, that it was important to go out a lot. About this time she met a man who attracted her, and now her feelings had an adult, independent character. After handling many difficulties admirably, she married him three months later. Her Willoughby score had dropped to 17. She had 14 interviews in all, and a year later was reported to be well and happy.

**CASE 6.**—Early in 1951 a divorcee of 39 stated that from as far back as she could remember she had been nervous and hypersensitive and perpetually worried about the future. Many ordinary situations, such as overhearing others quarrel, constituted stresses for her, made her anxious and left her fatigued, and sometimes produced epigastric pain. For seven years she had persistently suffered from fibrositic backaches. Her symptoms had improved somewhat after her divorce, two years previously.

She was encouraged to be more assertive and less subservient to the wishes of her friends. But her severest tensions arose from situations in which no direct action was possible, e. g., having visitors for dinner. Thus, from her seventh interview onward she was given lessons in relaxation. Her response was excellent. She became able to relax and to calm herself in an increasing range of situations, the anxiety-evoking power of which waned and eventually disappeared. The patient had 13 interviews over four months, during which she entirely overcame her neurotic nervousness and was functioning well in all areas. Her fibrositis disappeared completely after the first month. In a three-year follow-up there has been no recurrence but, instead, continued strengthening.

**CASE 7.**—A 23-year-old divorced tram driver entered the consulting room in a state of acute anxiety. Eight hours before a woman had walked into his slowly moving tram. She had been "knocked out and her head was bleeding." Although a doctor had told him that the woman's



## RECIPROCAL INHIBITION—PSYCHOTHERAPEUTIC EFFECTS

injury was not serious, he had become increasingly shaky and had developed severe epigastric pain. He had recovered from previous accidents in an hour or two, but in these no human injury had been involved.

The significance of the statement that no human injury was involved is that when the patient was 13 his father had died after an accident and since then he had had a fear of human blood. Even the tiny bead of blood that might appear on his face during shaving gave him an uncomfortable feeling. He was quite indifferent to animal blood—had seen oxen killed and had himself cut the throats of fowls. It was clear that his grossly excessive reaction to the present accident was due to his phobia for human blood, and to overcome this phobia was the central aim of therapy.

The first five interviews, which occurred over six days, were confined to obtaining an understanding of the patient's personality and background and to overcoming his immediate disturbed state by intense, hypnotically induced relaxation. At the fifth interview he reported feeling very well. He was told to drive a tram again for a short distance, which he did later that day, without any ill effect.

At the sixth interview various situations involving human blood were arranged in ascending order of their disturbing effect. From this time onward, at each interview, while the patient was in a state of hypnotic relaxation, he was made to visualize "blood situations." The feeblest was a slightly blood-tinged bandage lying in a basket. When this failed to disturb his relaxation, he was presented with a tiny drop of blood on his own face while shaving. In this way, with the presentation of two or three images at each session, it was possible gradually to work up to a stage at which the patient could visualize a casualty ward full of carnage and not be disturbed by it.

The significance of this method for real-life situations was revealed in this case in a most dramatic way. Two days before his last interview the patient saw a man knocked over by a motorcycle. The victim was seriously injured and was bleeding profusely. The patient was absolutely unaffected by the blood and, when the ambulance arrived, helped to load the victim on to it.

CASE 8.—A married woman of 32 came for treatment on March 23, 1953. She had been nervous and timid as long as she could remember. Rheumatic fever before puberty had been followed by chorea, which had improved very slowly at first, but not at all since the age of 16, and she had been left with persistently troublesome choreiform movements, which were worse during any emotional upset. In December, 1952, she had been injured in a motor accident and had spent three weeks in the hospital. There, as the pain of her injuries lessened, she noticed that she was very tense, that her twitchings were much worse, and that she had great difficulty in concentrating. These symptoms had been unremittingly present ever since. After her discharge from the hospital she had been specially anxious when in a car. This had improved a little through repeatedly forcing herself to go into cars and be driven around. But she still reacted with panic to every minor "threat" of an accident, e. g., if a driver 100 yards ahead were to fail to obey a "stop" sign, or if her husband took a bend "in a swerving way."

Treatment consisted, in the first place, in teaching her progressive relaxation. Her control of personal relations was also given attention, in particular the handling of her small son, which soon improved markedly. After a month's treatment (11 interviews) she was much better and had only occasional choreiform movements. But she was still reacting badly to motorcar situations. Hypnotic desensitization was then begun, and after 12 sessions of this, by the end of June she reported being completely unperturbed by all normal driving experiences. Her choreiform movements had almost stopped, and she said that never at any time, even in childhood, had she felt so well. On being interviewed in February, 1954, she stated that she had, if anything, continued to improve.

CASE 9.—A 47-year-old married male nurse, employed in an industrial first-aid room, was sent for psychiatric treatment by the medical officer who had observed him during the previous four years. For 17 years he had never been free from an uncontrollable impulse to mimic any rhythmic movements he saw, e. g., waving of arms and dancing. He would also automatically



obey any command, no matter from whom. A command, though, could not stop a rhythmic movement. The workmen frequently exploited his compulsion, to amuse themselves, often exhausting him and distressing him sometimes so much that he was left trembling.

No anxiety component could be observed in this compulsive behavior, but it was resolved to employ hypnosis to try to break the compulsion by attaching to the cues to its occurrence new and incompatible behavior. The patient was a good hypnotic subject, and six inductions were done in the course of three interviews. Two were done at the first interview. At the first induction he was made to recall the first occasions of compulsive mimicry and obedience, and was then given the direct suggestion that he would stop imitating. At the second he was simply hypnotized and awakened, as a control experiment. No change followed either of these trances.

At the second interview the posthypnotic suggestion was made that after waking he would copy only alternate movements of the therapist's right arm; but on being awakened, he still copied every movement, as before. He was then hypnotized again and told that on waking he would find that he would move only his hand when the therapist moved his whole arm rhythmically. This posthypnotic suggestion was obeyed. A third trance was induced in that session and the posthypnotic suggestion given that he would decrease his movement as the therapist continued to wave his arm rhythmically, and also a general suggestion that he would move only his right hand when impulses to mimic anybody arose. When he woke, his impulses did lessen.

At his third interview, two days later, the patient reported that he had entirely stopped being affected by other people's movements or commands. He showed no reaction at all to the therapist's beating his fist on the desk. He said that he was sleeping much better and was no longer startled at being awakened, and his fear of the dark had vanished. He was hypnotized again and told he would continue to be unaffected by people's movements or commands. During this trance, at the therapist's instigation, he told how the onset had followed a violent awakening by a nurse early one morning when he was in hospital with pneumonia.

Eighteen months later the patient was perfectly well and had not relapsed in any respect.

#### SUMMARY

The case is presented that conditioned inhibition founded on reciprocal inhibition is the basis of most fundamental psychotherapeutic effects. This principle is shown to explain a large number of widely used therapeutic methods and has led to some new methods, which are described. Of 122 patients treated by these methods, 110 were apparently cured or much improved. It is shown that certain other current theories are unable to account for the same range of facts as that subsumed by the reciprocal inhibition hypothesis.

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## PULMONARY ABSCESES IN A MENTAL HOSPITAL

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THE DISCOVERY of a pulmonary abscess in a patient in one of our services led us to begin an investigation of the total population and to review the available records to determine the relative incidence of this disorder in the Agnews State Hospital, to ascertain whether it were commoner here than in the general population, and, if so, to investigate those factors which might be involved in the production of this increased incidence. In a survey of all patients in the hospital on or hospitalized since October, 1952, we discovered 15 nontuberculous, pyogenic lung abscesses. With an average daily hospital population of about 4,500, this figure represents an incidence rate of 0.24% for this hospital population. Although no recent statistics are available, a comprehensive survey of hospital discharges in the City of New York in 1933 showed the incidence rate for that population to be 0.00145%, which is, perhaps, slightly higher than the rate in other available studies.\* With this figure as a representative morbidity rate of a normal population group, the incidence of lung abscess in this mental hospital would appear to be approximately 161 times the normal expectation. A rate so much above normal, we feel, bears further investigation. To aid in presenting and analyzing our data, we have added another case uncovered by us but occurring prior to October, 1952, in which the specific 17-month period was not a pertinent factor.

A review of the pertinent literature reveals several articles concerning lung abscess as a complication of electroshock therapy, the majority of which are in the foreign literature.† Only one comprehensive article appears in the American journals,<sup>3</sup> and this, too, is concerned with abscess as a complication of electroshock therapy. Two cases of single abscess in the course of electroshock therapy have been reported.‡ In one of these<sup>4</sup> the presence of oral infection before treatment was noted and was felt to be an important factor in the etiology of the abscess. Meduna and Friedman<sup>5</sup> reported a rate of 1% complicating shock therapy regardless of whether pentylenetetrazol (Metrazol) or electric shock was used, and Zeifert<sup>7</sup> reported on a group of cases occurring during pentylenetetrazol therapy. Kwalwasser, Monroe, and Neander<sup>6</sup> reported 25 cases occurring in 2,500 patients receiving electroshock therapy, a rate of 1%, the same as Meduna and Friedman's, and discussed the factors involved. After reviewing their cases, Kwalwasser and associates concluded that age, disturbed behavior, and poor dental hygiene were significant factors in the production of the abscesses. Since this is the only comprehensive

From Agnews State Hospital.

\* Personal communication: Letter from the Division of Public Health Methods, Department of Health, Education, and Welfare, United States Public Health Service, April 2, 1954.

† References 1 and 2.

‡ References 3 and 4.

study in the American literature, although still relating to shock therapy and not to total hospital population, we shall endeavor to compare and contrast our data with theirs.

Of the 15 patients in our study who developed lung abscesses in the 17-month period, 13 had received electric shock previously. During this period 2,326 patients received this form of therapy, providing, among the patients receiving shock, an incidence rate of 0.56%. This is nearly twice the rate in the total hospital population and about 386 times the normal morbidity rate. Although somewhat less than the 1% rate mentioned previously,<sup>§</sup> it is still very high and within the range quoted in a survey of the total reported incidence of abscess with electric shock.<sup>1</sup> Although

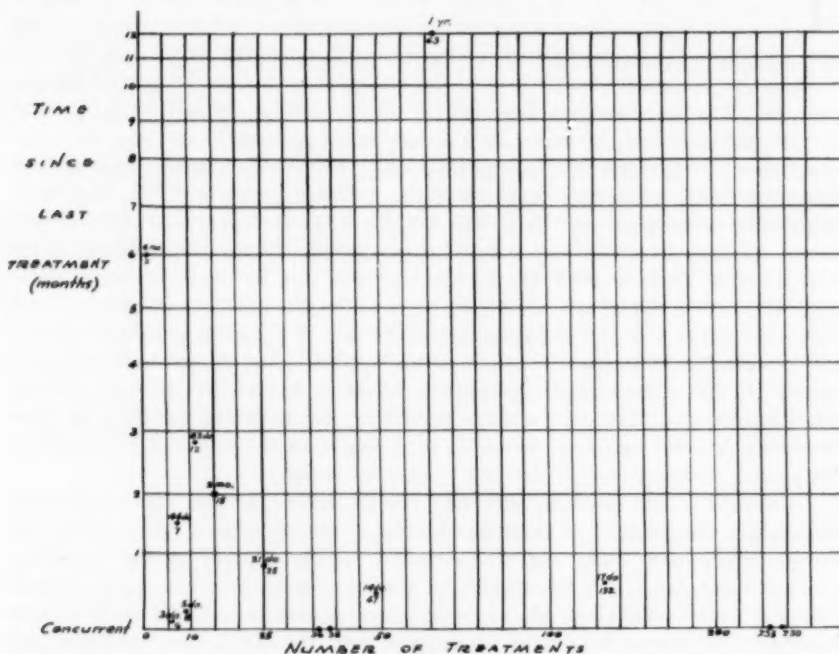


Chart 1

it is apparent from this finding that E. S. T. is a significant factor, it would be unwise to conclude that it was the only factor, or the most significant factor, in all the 13 cases.

Further study of these cases, plus the additional case mentioned above, shows that there was great variance in the number of prior treatments and in the time elapsed since the last treatment. Chart 1 shows the number of prior shock treatments plotted against the time from the last treatment. These data suggest that E. S. T. was an important factor in a majority of the cases, since in 12 of the 14 the complication occurred within three months of the last shock treatment. However, seven of the patients had 25 treatments or less, and four had 10 treatments or less, which findings would suggest that other factors beside E. S. T. were important in

<sup>§</sup> References 5 and 6.

# PULMONARY ABSCESES IN A MENTAL HOSPITAL

the causation of these abscesses. In comparison, Kwalwasser and co-workers<sup>5</sup> found that 3 patients of the 25 had less than five electroshock treatments.

A study of the ages of the patients reveals the age distribution to be as follows: one aged 26, seven from 30 to 39, three from 41 to 46, one 50, one 58, and three over 60, giving eight or 50%, over 40. Kwalwasser, Monroe, and Neander<sup>5</sup> found 15 over 40 years of age and decided that age was a significant factor, but it is difficult for us to reach that conclusion.

In our group eight abscesses were in the left lung, seven in the right lung, and one bilateral, a distribution which is rather unusual. Ten of the 16 abscesses occurred in women, but a slightly higher percentage of the hospital admissions and population is female.

An analysis of the 16 cases for duration of hospitalization prior to development of the abscess reveals generally amazingly long durations when compared with the

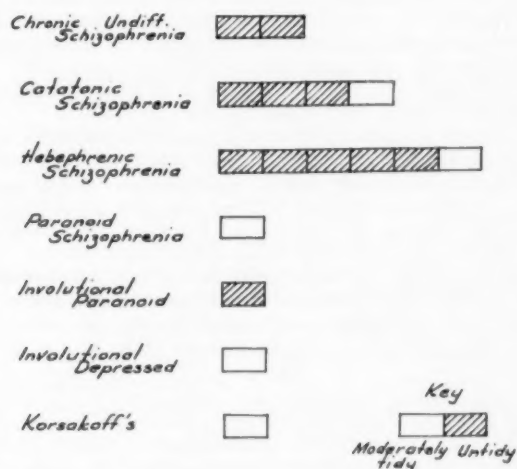


Chart 2.—Review of the diagnoses and conditions of the patients.

average. In this hospital the average patient stay is 4.6 months.|| A study of the 16 patients shows only 2 hospitalized less than 1 year, 3 between 1 and 2 years, 1 between 2 and 3 years, 2 between 3 and 4 years, 1 for 5½ years, and 5 over 10 years. In contradistinction, Kwalwasser and co-workers found 12 of their 25 patients hospitalized less than four months; still, they had 6 patients hospitalized over five years.

A review of the diagnoses and conditions of the patients (Chart 2) shows that of the 16 patients 11 were in poor condition, with untidiness and poor hygiene combined with withdrawal or assaultive behavior. Five were in fair condition, with at least a reasonable degree of self-care with encouragement. None demonstrated much spontaneity in effecting personal care. Of the 16 patients, 13 were schizophrenic and only 1 had a diagnosis of an organic brain syndrome. Fifteen of the 16 had diagnoses of psychoses. Although we have no definite statistics, it is our general impression that these figures do not reflect the proportionate admission ratio, which represents a much higher ratio of organic brain syndromes. These findings, corre-

|| Personal Communication.



spond closely with those of Kwalwasser, Monroe, and Neander,<sup>5</sup> who found 17 of their 25 patients with diagnoses of schizophrenia and 22 of the 25 untidy.

Two typical cases illustrating the behavior, length of hospitalization, etc., are presented here in summary:

**CASE 1.**—E. H., 46-year-old married woman of Mexican descent—onset in 1938 with visual and auditory hallucinations and a suicidal attempt by ingestion of a caustic solution as presenting symptoms.

Patient was the youngest in a sibling group of four. She was born in Mexico, and her father left the home during her infancy. The mother and children moved to California as migratory laborers. Patient had minimal formal educational training, resided in a Spanish-speaking community, and English is limited to meager phrases. Family economic adjustment was always marginal. She was married to a man of similar socioeconomic background in late adolescence and was the mother of seven children at time of her admission, with the oldest 12 years and the youngest 7 months.

Initially, the patient is described as unresponsive, autistic, actively hallucinated—both aurally and visually—affect shallow, inappropriate. She was placed in the diagnostic category of hebephrenic schizophrenia.

Her early hospital course was complicated by surgical care of an esophageal stricture, during which time her psychiatric status was stabilized at a more comfortable behavioral picture. She was pleasant, accessible; she was aware of personal needs and cared for herself satisfactorily; although still hallucinating, did not react to them so floridly.

The course of her illness has been that of steadily progressive regression, marked by increasing seclusiveness, disinterest, apathy, negativism, with periods of destructive, assaultive, and self-mutilating behavior. She required increased supervision in dressing, eating, bathing, etc. It was at this time, some 14 years after onset of illness, that electroshock therapy was instituted, with the limited aim of increasing her comfort and attaining a better behavioral adjustment. The therapy was effective. Patient became nondestructive; self-mutilation ceased. She began to participate in occupational therapy activities on the ward, smiled appropriately but shyly, and on occasion instigated interaction with ward technicians. Administration of the treatment was stopped because of the development of a lung abscess after the 10th treatment. During medical care of the abscess her ward behavior reverted to the original regressed condition previously described.

**CASE 2.**—H. K., a Negro man, admitted to the Agnews State Hospital on Nov. 1, 1951, at the age of 28, with a history of recurrent peculiar behavior for the previous several years. Present episode began one month prior to admission with religious preoccupation, bizarre behavior, and irrational activity. Examination revealed a silent, withdrawn, posturing, resistive man. Physical examination revealed an old fracture deformity of the left elbow. Patient was transferred to the acute treatment ward and began electroshock therapy on Nov. 7, 1951. After 21 treatments patient was in better contact, but paranoid, confused, affectless, and showed no improvement. Treatment was stopped, and patient was transferred to an observation ward. In February, 1952, patient made a suicide attempt. He was transferred in April, 1952, to a chronic, tidy ward, where he showed continued slow improvement but was generally mute and indifferent, although cooperative and able to assist on the ward. However, patient slowly began to relapse into a more catatonic, unresponsive state and was transferred to the chronic treatment ward. As he continued to show signs of deterioration, untidiness, etc., shock therapy was reinstituted in July, 1953. For the next several months patient received several short courses of shock therapy and responded to each with verbalization and increased interest in self and environment. During the third of these series, while patient was unresponsive, mute, and only moderately tidy, it was noted that he began to spit blood after electroshock. Physical examination was normal, but chest x-ray revealed an abscess of the right lung. Patient was transferred to the medical ward, where treatment for this condition was begun.

#### COMMENT

Any acceptable explanation which offers to explain or to suggest factors involved in the markedly increased incidence of lung abscess in state mental hospitals would appear, from the above data, to have to take into account the following factors: (1)



the high number of patients receiving E. S. T. in the group; (2) the apparently poor psychiatric condition in the majority of patients in whom this malady develops, and (3) the high proportion of psychotics in whom this illness develops as compared with the total population.

Zeifert,<sup>7</sup> in reviewing the incidence of lung abscess in patients receiving pentylene-tetrazol therapy, concluded that these abscesses were secondary to infarctions occurring as a result of emboli and that these emboli were related to the intravenous injection of the chemical. He noted that the onset in those cases was sudden, dramatic, and directly related, temporally, to the injections. It is doubtful, however, whether infarction is a factor in our cases. First, no evidence of thrombosis, embolism, or infarction has been noted at autopsy. Second, contrary to Zeifert's cases, the general mode of onset in our patients was subtler and more insidious, and, indeed, there is reason to believe that many were present for some time before discovery.

Meduna and Friedman<sup>8</sup> are quoted as emphasizing the role of aspiration in the etiology of lung abscesses. Rubin,<sup>9</sup> in discussing this disorder, lists as primary factors in the etiology poor oral hygiene and carious teeth, and aspiration of vomitus with coma or spontaneous aspiration. Our conclusions closely parallel those of Kwalwasser, Monroe, and Neander, which were previously mentioned.

However, in considering the basic etiological factors involved in the production of lung abscesses, several contradictory points must be borne in mind. Although poor oral hygiene combined with E. S. T. seems to be the important factor in the production of lung abscesses, some observations we have made seem to indicate, perhaps, another basic factor. In this hospital by far the greatest number of E. S. T.'s are given on the acutely disturbed wards—a far greater number, in fact, than on the chronic wards, from which most of the patients in the present study come. Subsequent to the beginning of this study, empirical observations were made on the oral hygiene of the patients receiving E. S. T. on the acute wards, and the conclusion was drawn that there were certainly enough carious teeth among the perhaps 150 or more patients being treated each week on the acute wards to produce a significant number of abscesses if there were no factors other than oral hygiene and E. S. T. involved. Yet, of the 16 cases herein reported only 1 was from an acute treatment ward. Treatment techniques are standard throughout the hospital, and it is not infrequent for patients to receive 30, 40, 50, or more treatments on the acute wards; therefore this apparent discrepancy cannot, we believe, be laid to premature removal of the patients from the acute wards.

The concept of an oral focus of infection supplying material for aspiration with E. S. T. and implantation in a pulmonary nidus in the origin of lung abscess, as presented by previous authors, seems logical but incomplete. A third factor, that of the resistance of the patient involved, must be considered. That there is some difference between the chronic and the more acutely ill patients is apparent from the above data, and that this difference is in the sphere of resistance to infection seems logical to us. In general, psychosis is said to be a disease of the individual as a whole. It is with this concept in mind that we must view the formation of lung abscess.

Investigators in the past several years<sup>¶</sup> studying the physiology of schizophrenics have noted that in patients with chronic long-term schizophrenia there is

¶ References 9 through 11.

a decrease in general physiological activity as well as in psychic and motor activity. The clinical concomitants of these theoretical postulates derived from experimental data are found, we believe, in the patients included in this study. That no similar findings of lowered biological responsivity have been found in the more acutely ill is, no doubt, an important factor in the finding of lung abscesses in only two patients hospitalized less than one year.

It would, we believe, be of interest to study the incidence of abscess formation in patients receiving E. S. T. on a brief inpatient or outpatient basis. This study suggests that the incidence would be much less than herein observed.

It is also suggested by these studies that in chronic patients who are started on E. S. T. a thorough prior dental examination and a concomitant course of a chemotherapeutic agent might be useful as prophylactic measures.

#### SUMMARY AND CONCLUSIONS

Sixteen cases of lung abscesses in a state mental hospital are reported. Fifteen of these occurred in a 17-month period beginning October, 1952. All but two patients received E. S. T. during their hospitalizations. These incidence rates are 0.24% and 0.56%, respectively, as compared with a normal morbidity rate of 0.00145%.

The 16 cases are discussed and common factors derived and compared with those noted in the literature.

From the data presented, the importance of electric shock and poor oral hygiene in the causation of lung abscesses in these patients is apparent. This conclusion is in agreement with most of the literature.

In addition, we feel that the chronic psychosis itself, like any other chronic disease process, produces diminished body defenses and resistances to invasion by infectious agents and that this decreased resistance represents a third, and equally important, factor.

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## PATTERNS OF PERCEPTUAL ORGANIZATION WITH SIMULTANEOUS STIMULI

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**S**TUDIES of function of the nervous system by any one method will show patterns. This is a general law which applies to motor, perceptual, and psychic functions. Patterns of functions are present in the normal as well as in the abnormal state. For example, normal subjects show variations in the ability to discriminate two closely applied points in different regions of the body. Thus, the pattern for two-point discrimination is one in which the finest differentiation is at the tongue or finger tips, while other parts of the body, such as the back or the thigh, require a greater distance between two points before discrimination of "twoness" can be made.<sup>1</sup> According to Pearson<sup>2</sup> the pattern for the normal sense of vibration is one in which the threshold is low at the clavicle and high over the sacrum. In vision discrimination of targets under daylight illumination is best in the central, and poorest in the peripheral, portion of the perimetric field. And so it is with all other modalities. Each sensation has a pattern in space as well as in time. Each of these patterns is obtained by adopting procedures in which a single stimulus figure is used in testing the subject.

In measuring sensation, we know that there are many factors which influence the perceptual response. Intensity and duration of stimulus, the stimulus figure, the locus in the sensory field, the attention and intellectual capacity of the subject are but a few of the determinants. Recently we have stressed symmetry as having a bearing on perception.<sup>3</sup> Still another factor is age.<sup>4</sup> For instance, there are some perceptual examinations which could not be carried out in children because the ability to respond to these tests depends partly on the ability to concentrate on a particular problem and to cooperate over a matter of many minutes. These are two properties which most very young children do not possess. Moreover, we have found that reactions in the old are not the same as those in the younger subjects.

Another condition which influences the perceptual response is the number of stimuli employed at one time. Two stimuli when applied simultaneously may yield responses which are different from those to stimuli applied in succession. Simultaneous touch of the face and hand may be perceived only on the face, whereas when each of these parts is successively touched with an interval of one or more

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seconds, the same subject perceives each stimulus. The simultaneous application of more than two stimuli may yield other types of perceptual reactions. Cohn<sup>5</sup> applied three stimuli all at once and obtained results which were different from those elicited with conventional single stimuli in the same areas. In 1893 Krohn<sup>6</sup> investigated the effects of simultaneous touch stimulation of multiple (seven) regions of the skin in normal subjects. Parts of the trunk, extremities, forehead, and, at times, the chin were touched simultaneously by tambours. With these tests the subjects made errors in localization of the applied stimuli. However, no distinct pattern was sought. In analyzing Krohn's material, we found a suggestion of a pattern in that there were less errors over the back than over the front. This study was interesting but not very illuminating.

The technique of double simultaneous stimulation had been known since the time of Hippocrates. In 1882 Oppenheim<sup>7</sup> mentioned the method in his textbook. Since this description there had been few intensive studies of the method until 1943, when one of us began a series of investigations. During the past decade we have examined several thousands of subjects with this technique. As we gathered our data, it was noted that in tests involving asymmetrically placed stimuli certain regions of the body yielded correct responses, while others yielded consistently incorrect responses. On numerous simultaneous stimulations of the face and hand a distinct pattern of response has been observed in which errors in identifying and localizing the stimuli on the hand became apparent. Conversely, there were very few errors in perception of the stimuli on the face. In this test situation the face was "dominant" to the hand. Face dominance has been found in normal adults, but it is particularly evident in patients with disease of the brain, in very aged persons, and in normal children, 3 to 6 years of age. This pattern of response, namely, face dominance, has been found so consistently that it prompted us to study body combinations other than that of the face and hand. The object of this investigation was to determine the order of dominance when various combinations of two parts of the body were tested in this manner. A preliminary note on this study was reported at the 76th Annual Meeting of the American Neurological Association, in June, 1951.<sup>8</sup>

#### METHOD AND SUBJECT MATERIAL

The method of testing was the same as that described for the face-hand test in previous communications.<sup>9</sup> The subject was requested to close his eyes, and two parts of the body were simultaneously touched or stroked. He was asked what he felt and to localize the stimuli. If only one stimulus was reported, the subject was then asked if another was felt.

The subjects used in these studies consisted of patients and normal adults and children. Series I: Patients who showed mental changes or an organic mental syndrome\* as a result of disease of the brain, such as arteriosclerotic encephalopathy, senile psychosis, severe cerebral trauma, Alzheimer's disease, toxic encephalopathy, or brain tumor. In general, patients with severe mental changes who made many errors on simultaneous stimulation tests were chosen for a special study group. Patients with aphasia, hemiparesis, or a hemisensory defect were included in another group. Series II: Normal children and adults. The normal children were taken from a day-care center and an orphanage. The normal adults were patients on the wards of the general hospital, those attending hospital clinics, and Army inductees. None of the normal

\* The mental changes which make up the organic mental syndrome consist of a combination of at least three or more of the following manifestations: impairment in orientation, memory, calculation, or general information; rigidity and concreteness in mental performance, and marked fluctuations and inability to perform when there is more than one aspect to a situation.

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children or normal adults had manifest disease of the nervous system. They had not been previously examined by the method of double simultaneous stimulation. We also examined a group of older people. These were presumably normal, although cerebral arteriosclerosis could not be entirely excluded in people between the ages of 65 and 90 years. Series III: Patients with schizophrenia or manic depressive conditions. These patients were adults in the wards of the Bellevue Psychiatric Hospital and Manhattan State Hospital. No attempt was made to study the specific types of schizophrenia. Most of them were of the paranoid, mixed, or simple schizophrenic varieties.

Inasmuch as previous investigations have shown that patients with severe mental changes due to disease of the brain and normal young children made frequent errors in tests of simultaneous stimulation, it was natural that we should make the most extensive studies on these two groups.<sup>10</sup> Also, since normal adults make few errors after the first two to three trials on double simultaneous stimulation, it was not possible to detect a pattern in these subjects.

From these three series of cases we studied several groups in detail. Group A, which was studied in the greatest detail, consisted of 20 patients with organic mental syndrome (10 males and 10 females). These subjects were tested with the method of double simultaneous stimulation of different parts of the body and in multiple combinations. The following parts of the body were examined: face, shoulder, hand, back, breast, penis, pubic region in females, buttock, thigh, and foot. Patients were tested while they were completely nude and, for the most part, while they were standing. The specific areas stimulated for certain parts of the body were as follows: the dorsum of the hand; the dorsum of the foot; the anterior aspect of the thigh; just below the scapula on the back; close to the midline on the buttock; the nipple and areolar area of the breast; the lower quadrant of the abdomen; the tip of the penis or the mons veneris. Of these body parts there were 45 possible double combinations. It should be noted that the combinations were of regions distributed along the longitudinal axis of the body. Each patient was tested in all 45 combinations in a random but similar order. Twelve tests were done for each combination. These consisted of five tests of the two body parts in a homolateral relation, five tests of the two body parts in a heterologous relation, and two tests in a homologous relation, one for each of the body parts. There were 240 tests in every combination for the total group. Each patient received 540 tests.

The other group, Group B, which we studied in great detail, using thousands of trial tests, consisted of 40 normal children between 3 and 6 years of age. In 20 of these children (12 boys and 8 girls), all body combinations of two were tested except those involving the genital zone. In the other 20 children (12 boys and 8 girls), the genital region combinations were tested as well as some of the other body combinations. The testing was carried out in the same manner as described for patients with disease of the brain except that only half as many tests in each combination were done. The genital zone was usually touched directly, with the child partially nude. The remaining unexposed body parts were usually tested through the clothing.

To supplement these studies, we also examined a group of 692 normal adults, 605 schizophrenic adults, and 664 patients with organic mental syndrome. However, these subjects were not tested as intensively as those of the above two groups. Different body combinations were tested in different subjects. Only one of the following body combinations was tested in any one subject for 10 trials or more; face-hand, face-breast, face-penis, face-back, face-foot, face-shoulder, shoulder-hand, breast-hand, penis-hand, thigh-hand, foot-hand, thigh-foot, breast-foot, breast-thigh, buttock-foot, penis-foot, shoulder-foot, and shoulder-breast. The two parts of the body were first touched in two heterologous relations and then in the two homolateral relations. Particular attention was directed to the first response. If an error was made in any one test, that particular test was repeated until the patient was correct, or for at least five times if the error persisted. At least 10 trials were done on each patient. Stimulation of the unexposed parts of the body, except for the penis, was done through clothing. The penis was touched directly.

The pattern of dominance has also been studied incidental to other investigations on perception in groups such as Group C, comprised of patients with focal brain disease manifested by hemiplegia or aphasia<sup>11</sup>; Group D, patients with long-standing or congenital blindness; Group E, patients who had congenital or long-standing deafness; Group F, normal adults recovering from general anesthesia or while under the effect of intravenous amobarbital (Amytal) sodium<sup>12</sup>; Group G, psychiatric patients receiving electroconvulsive therapy; Group H, mentally

defective adults,<sup>13</sup> and Group I, very aged or senile adults.<sup>4</sup> It must be emphasized, however, that we did not test all the possible combinations of body parts in every one of these groups except in Groups A and B. The emphasis was mainly on determining the relationship of the face and the hand to the rest of the body areas. The results obtained in these incidental studies showed that the pattern of dominance was similar to the one obtained in this study of patients with severe mental changes due to disease of the brain.

## RESULTS

The responses on double simultaneous testing of any two parts of the body fell into several groups. Using the face-hand combination as an example, the subject may report the following responses, as recorded in Table 1.

Responses in which there was extinction or displacement † of the stimulus over one area in any combination were tabulated as a single type of response. For example, in the face-hand combination responses in which the face stimulus was correctly perceived but in which extinction or displacement of the hand stimulus

TABLE 1.—*Pattern of Responses to Double Simultaneous Face-Hand Tests*

Combination of Body Parts	Possible Response	Classification	Dominance
Simultaneous touch of face and hand	(a) Face-hand	Correct	None
	(b) Face only	Extinction	Face
	(c) Hand only	Extinction	Hand
	(d) Face-face	Displacement	Face
	(e) Hand-hand	Displacement	Hand
	(f) Face-other part of body	Displacement	Face
	(g) Hand-other part of body	Displacement	Hand
	(h) Face-and a part in space	Exosomesthesia	Face
	(i) Hand-and a part in space	Exosomesthesia	Hand

occurred were tabulated together under "face" responses. Each of the responses indicates dominance of the face over the hand. Hence, the reason for grouping them under "face dominance." Face dominance responses were much more frequent than any of the hand dominance responses.

The responses for all the body combinations were tabulated in a similar manner. For the patients with organic mental syndrome and for the normal children tested in all body combinations, the "dominant" responses for one part of the body as compared with those of the other part of the body in each combination were analyzed by the *t* test. The initial responses of the normal and schizophrenic adults and of the other patients with organic brain disease tested in a single combination were analyzed by the method of chi-square. There were a small number of responses

† The failure of the subject to report one of two simultaneously applied stimuli has been called "the phenomenon of sensory extinction," or "extinction." The part of the body where the stimulus is perceived is said to be "dominant" to the part of the body where the simultaneous stimulus is not perceived. When the subject reports two sensations but mislocalizes one of them, the "displacement" of a percept is said to have occurred. Displacements are usually in the direction of the dominant stimulus and may be partial or complete. Occasionally, one or both stimuli are displaced into the extrapersonal space. This has been termed "exosomesthesia."<sup>14</sup>



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TABLE 2.—Responses of Twenty Patients with Organic Mental Syndrome to Simultaneous Tests of Different Body Combinations

Face Combinations			Dominant Responses	
	Total Errors*		Face	Other Part
Face-genitals.....	68	37	31	
FACE-abdomen †.....	109	78	31	
FACE-buttock.....	79	60	19	
FACE-breast.....	122	104	18	
FACE-foot.....	89	66	23	
FACE-back.....	105	95	10	
FACE-shoulder.....	154	127	27	
FACE-thigh.....	104	85	19	
FACE-hand.....	149	145	4	
Genitals Combinations			Dominant Responses	
	Total Errors		Genitals	Other Part
Genitals-face.....	68	31	37	
GENITALS-abdomen.....	121	92	29	
GENITALS-buttock.....	78	66	12	
GENITALS-breast.....	106	84	22	
GENITALS-foot.....	138	115	23	
GENITALS-back.....	98	83	15	
GENITALS-shoulder.....	90	70	20	
GENITALS-thigh.....	124	94	30	
GENITALS-hand.....	143	132	11	
Hand Combinations			Dominant Responses	
	Total Errors		Hand	Other Part
Hand-FACE.....	149	4	145	
Hand-GENITALS.....	143	11	132	
Hand-ABDOMEN.....	152	21	131	
Hand-BUTTOCK.....	152	23	109	
Hand-BREAST.....	163	29	134	
Hand-FOOT.....	136	19	117	
Hand-BACK.....	97	28	59	
Hand-SHOULDER.....	127	20	107	
Hand-THIGH.....	142	28	114	
Abdomen Combinations			Dominant Responses	
	Total Errors		Abdomen	Other Part
Abdomen-FACE.....	109	31	78	
Abdomen-GENITALS.....	121	29	92	
Abdomen-buttock.....	90	61	38	
Abdomen-breast.....	111	55	56	
Abdomen-foot.....	104	46	58	
Abdomen-back.....	97	44	53	
Abdomen-shoulder.....	90	58	32	
Abdomen-thigh.....	115	76	39	
ABDOMEN-hand.....	152	131	21	
Buttock Combinations			Dominant Responses	
	Total Errors		Buttock	Other Part
Buttock-FACE.....	79	19	60	
Buttock-GENITALS.....	78	12	66	
Buttock-abdomen.....	90	38	61	
Buttock-breast.....	94	55	39	
Buttock-foot.....	118	43	75	
BUTTOCK-back.....	104	79	25	
BUTTOCK-shoulder.....	93	65	28	
Buttock-thigh.....	105	45	60	
BUTTOCK-hand.....	132	109	23	
Breast Combinations			Dominant Responses	
	Total Errors		Breast	Other Part
Breast-FACE.....	122	18	104	
Breast-GENITALS.....	106	22	84	
Breast-abdomen.....	111	56	55	
Breast-buttock.....	94	29	55	
Breast-foot.....	100	50	41	
BREAST-back.....	77	55	22	
Breast-shoulder.....	121	52	69	
Breast-thigh.....	85	48	37	
BREAST-hand.....	163	134	29	
Foot Combinations			Dominant Responses	
	Total Errors		Foot	Other Part
Foot-FACE.....	89	23	66	
Foot-GENITALS.....	138	23	115	
Foot-abdomen.....	104	58	46	
Foot-buttock.....	118	75	43	
Foot-breast.....	160	41	59	
Foot-back.....	105	49	56	
Foot-shoulder.....	96	51	45	
Foot-thigh.....	125	77	48	
FOOT-hand.....	136	117	19	
Back Combinations			Dominant Responses	
	Total Errors		Back	Other Part
Back-FACE.....	105	10	95	
Back-GENITALS.....	98	15	83	
Back-abdomen.....	97	53	44	
Back-BUTTOCK.....	104	25	79	
Back-BREAST.....	77	22	55	
Back-foot.....	105	56	49	
Back-shoulder.....	131	78	53	
BACK-thigh.....	127	86	41	
BACK-hand.....	97	69	28	
Shoulder Combinations			Dominant Responses	
	Total Errors		Shoulder	Other Part
Shoulder-FACE.....	154	27	127	
Shoulder-GENITALS.....	90	20	70	
Shoulder-abdomen.....	96	32	58	
Shoulder-BUTTOCK.....	93	28	65	
Shoulder-breast.....	121	69	52	
Shoulder-foot.....	96	45	51	
Shoulder-back.....	131	53	78	
Shoulder-thigh.....	93	58	35	
SHOULDER-hand.....	127	107	20	
Thigh Combinations			Dominant Responses	
	Total Errors		Thigh	Other Part
Thigh-FACE.....	104	19	85	
Thigh-GENITALS.....	124	30	94	
Thigh-abdomen.....	115	39	76	
Thigh-buttock.....	106	60	45	
Thigh-breast.....	85	37	48	
Thigh-foot.....	125	48	77	
Thigh-BACK.....	127	41	86	
Thigh-shoulder.....	93	35	58	
THIGH-hand.....	142	114	28	

\* Two hundred tests done in each combination were analyzed statistically. The remaining 40 tests in each combination were of homologous body parts and did not lend themselves to this type of analysis.

† Capital letters indicate dominant part as evidenced by a *t* test value of 5% or less.



which were difficult to interpret, and there were a few that showed characteristic perseveration in behavior. These responses were not included in the statistical analysis.

Extinction and displacement occurred in all of the body combinations tested in all groups. The incidence of these phenomena varied with the method of testing. On testing body parts in a heterologous but bilateral relation, extinction and displacement occurred with approximately equal frequency. With tests involving ipsilateral body parts, the majority of errors consisted of extinction.

1. *Patients with Organic Mental Syndrome.*—In Group A 20 patients were tested in all the combinations of the body; there were 27 combinations in which the difference in the frequency of extinction and that of displacement in the two body parts tested was statistically significant, as evidenced by a *t* test value of 5% or less (Table 2). This difference occurred in combinations of the face and

TABLE 3.—Response on the Initial Trial in Patients with Organic Mental Syndrome Tested in a Single Body Combination

Combination of Body Part		No. of Subjects	Correct	Responses Indicating Dominance of Body Part		Other Responses
A	B			A	B	
FACE *	Hand	156	15	136	5	..
FACE	Breast	71	17	44	6	4
FACE	Penis	30	8	21	1	0
FACE	Back	30	7	17	2	4
FACE	Foot	30	9	21	0	0
SHOULDER	Hand	32	12	17	1	2
BREAST	Hand	51	7	37	5	2
PENIS	Hand	31	6	23	2	0
FOOT	Hand	49	10	30	7	2
THIGH	Hand	23	8	15	0	0
FOOT	Thigh	60	19	25	12	4
BUTTOCK	Foot	35	5	21	8	1
PENIS	Foot	40	8	30	1	1
Shoulder	Foot	23	1	12	9	1
Shoulder	Breast	13	3	5	5	0

\* Capital letters indicate dominant part as evidenced by a chi-square value of 5% or less.

other parts, the genital region (penis in males and pubic region in females) and other parts, or the hand and other parts. In combinations involving the face or the genital region, errors in perception were infrequent. Therefore the face and the genital region may be termed as dominant to all other parts of the body. In combinations involving the hand, the opposite phenomenon occurred; errors in perception were more frequent in the hand. The hand may be classified as the least dominant area of the body. Thus, in face-hand tests the results may be expressed either as degree of face dominance or that of hand errors. There were four additional combinations in which dominance was manifested. The buttock was dominant to the back and shoulder, the breast was dominant to the back, and the back was dominant to the thigh. The remaining 18 combinations showed no dominance between the two body parts tested, as evidenced by *t* values greater than 5% (Table 2). These 18 combinations were retested in a different group of 20 patients. The method was similar to that described previously except that the order of testing was more randomized. When the statistical probabilities of the two series of tests were combined, all of these combinations again failed to manifest dominance.

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An analysis of the responses of the group of 664 patients with organic mental syndrome tested in single rather than multiple body combinations showed a similar pattern (Table 3). There were no instances in which dominance in this group was different from that of the preceding group. However, some combinations manifested dominance which was not shown in the first group. Thus, the face was dominant to the genital region; the foot was dominant to the thigh, and the buttock was dominant to the foot.

In summary, the foregoing results show that double simultaneous stimulation tests of parts of the body exhibit a definite relationship of one part to another. This is manifested by varying degrees of dominance, which may be considered as a gradient of sensation. At the top of the gradient is the face, the most dominant part of the body. The genital region is slightly less dominant than the face but is dominant over all other parts of the body and is thereby the next body area in the order of dominance. At the other end of the gradient is the hand, the least dominant part of the body. The remaining areas of the body fall in the gradient between the

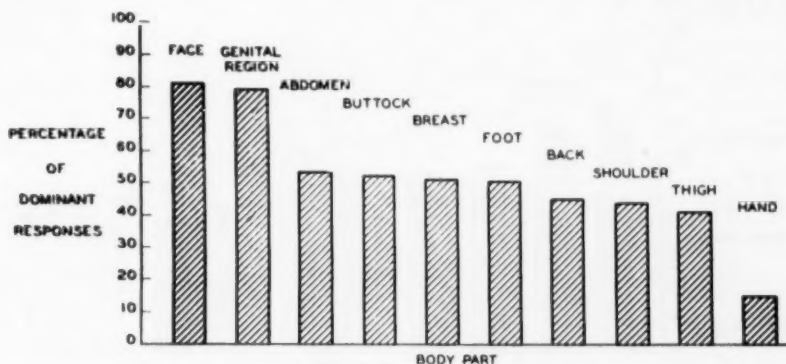


FIG. 1. ORDER OF DOMINANCE IN PATIENTS WITH ORGANIC BRAIN DISEASE

face and genital region and the hand. These parts include the shoulder, foot, thigh, and the areas on the trunk. When tested in combination with each other, these body parts failed, for the most part, to yield differences in dominance among one another. There was a tendency, however, for the buttock, abdomen, breast, and foot to be dominant to the back, shoulder, and thigh. The order of dominance of all body areas may be illustrated by comparing the total number of dominant responses for each area in the group of 20 patients tested in multiple combinations (Fig. 1).

2. *Normal Children.*—It has been shown that normal children make errors in simultaneous cutaneous sensory tests just as do patients with an organic mental syndrome. There was one striking difference, however, between the two groups. Children tended to learn the correct response as the tests were repeated over a period of days, whereas patients with an organic mental syndrome showed but temporary learning tendencies. They soon forgot what they learned and again made the errors.

When various combinations of two parts of the body were tested in the young children, an order of dominance became apparent, just as in the patients with an

organic mental syndrome. The order of dominance in normal children resembled, to a considerable extent, that found in patients with diffuse brain disease. The face was the most dominant and the hand the least dominant area (Fig. 2). The genital region was not so dominant as in patients with organic disease of the brain, since it failed to show dominance to the shoulder, back, and breast, although it was dominant to all other areas. In tests involving the genital region many children snickered, laughed, or showed other signs of special awareness of the sexual organs. Some refused to be touched there and became uncooperative. Because of this attitude, it was necessary to obtain the parents' permission for the test.

The order of dominance for the rest of the body areas in these children also showed little difference from that noted in patients with disease of the brain (Table 4). In only one of these combinations was dominance different from that demonstrated in patients with an organic mental syndrome. In children the foot was dominant to the buttock. The same combination tested in the group of patients with an organic mental syndrome showed the buttock dominant to the foot.

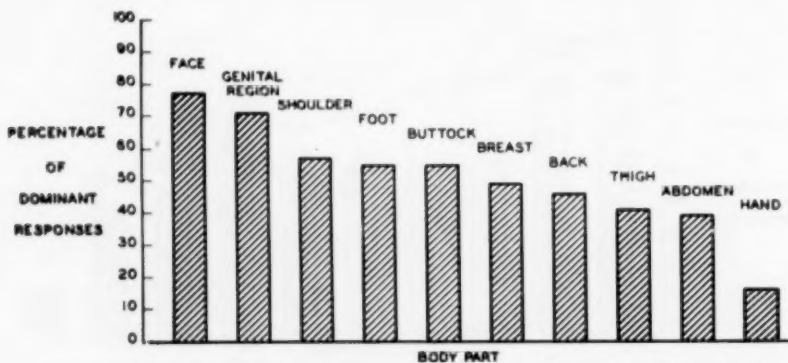


FIG. 2. ORDER OF DOMINANCE IN NORMAL CHILDREN 3-8 YEARS OF AGE

3. *Normal Adults.*—Several groups of normal adults were studied. In previous communications the responses of simultaneous touching of the face and hand were reported. The results showed a high face dominance. Examination of other body combinations showed a tendency to similar pattern, as recorded in the foregoing paragraphs (Table 5). However, the data obtained in combinations other than the face-hand were not very reliable, because the number of experiments were too few in number. It should be noted that the normal adult very readily grasps the idea of "twoness," or the concept that two stimuli are being used. Consequently, his chances of yielding a single response on repeated tests are small, especially if he once correctly reports the perception of the stimuli. Thus, it would be most difficult for us to get a large number of statistically significant data for other body areas.

In order to obtain reliable data it would be necessary to test a very large number of normal adults by statistical methods. For the time being, most of our emphasis was placed on testing patients with organic brain disease, young children, and very old adults. Judging from our data, it may be presumed that the complete order of dominance observed in patients with organic disease would also be present in the normal subject if a greater number of subjects were tested.

# PATTERNS IN PERCEPTION—SIMULTANEOUS STIMULI

TABLE 4.—Responses of Normal Children Three to Six Years of Age to Simultaneous Tests of Different Body Combinations

Face Combinations	Total Errors*	Dominant Responses	
		Face	Other Part
FACE-genitals †.....	57	38	19
FACE-shoulder.....	79	65	14
FACE-buttock.....	52	35	17
FACE-foot.....	77	65	12
FACE-breast.....	74	65	9
FACE-back.....	74	55	19
FACE-thigh.....	47	38	9
FACE-abdomen.....	66	51	15
FACE-hand.....	71	64	7
Genitals Combinations	Total Errors	Dominant Responses	
		Genitals	Other Part
Genitals-FACE.....	57	19	38
Genitals-shoulder.....	56	28	28
GENITALS buttock.....	65	45	20
GENITALS-foot.....	87	78	9
Genitals-breast.....	74	46	28
Genitals-back.....	62	39	23
GENITALS thigh.....	81	65	16
GENITALS abdomen.....	81	65	16
GENITALS-hand.....	88	79	9
Hand Combinations	Total Errors	Dominant Responses	
		Hand	Other Part
Hand-FACE.....	71	7	64
Hand-GENITALS.....	88	9	79
Hand-SHOULDER.....	66	7	59
Hand-BUTTOCK.....	72	5	67
Hand-FOOT.....	72	9	63
Hand-BREAST.....	79	17	62
Hand-BACK.....	85	15	70
Hand-THIGH.....	76	27	49
Hand-ABDOMEN.....	86	15	71
Shoulder Combinations	Total Errors	Dominant Responses	
		Shoulder	Other Part
Shoulder-FACE.....	79	14	65
Shoulder-genitals.....	56	28	28
Shoulder buttock.....	67	25	42
Shoulder-foot.....	63	31	32
SHOULDER-breast.....	77	56	21
SHOULDER-back.....	84	55	29
SHOULDER-thigh.....	59	39	20
SHOULDER-abdomen.....	74	48	26
SHOULDER-hand.....	66	59	7
Buttock Combinations	Total Errors	Dominant Responses	
		Buttock	Other Part
Buttock-FACE.....	52	17	35
Buttock-GENITALS.....	65	20	45
Buttock-shoulder.....	67	42	25
Buttock-FOOT.....	66	21	45
Buttock-breast.....	59	30	29
BUTTOCK-back.....	76	49	27
Buttock-thigh.....	66	31	35
BUTTOCK-abdomen.....	56	40	16
BUTTOCK-hand.....	72	67	5
Foot Combinations	Total Errors	Dominant Responses	
		Foot	Other Part
Foot-FACE.....	77	12	65
Foot-GENITALS.....	87	9	78
Foot-shoulder.....	63	32	31
FOOT-buttock.....	66	45	21
Foot-breast.....	61	32	29
Foot-back.....	66	31	35
FOOT-thigh.....	65	47	18
FOOT-abdomen.....	57	40	17
FOOT-hand.....	72	63	9
Breast Combinations	Total Errors	Dominant Responses	
		Breast	Other Part
Breast-FACE.....	74	9	65
Breast-GENITALS.....	74	28	46
Breast-SHOULDER.....	77	21	56
Breast-buttock.....	59	29	30
Breast-foot.....	61	29	32
BREAST-back.....	64	42	22
Breast-thigh.....	50	26	24
BREAST-abdomen.....	64	47	17
BREAST-hand.....	79	62	17
Back Combinations	Total Errors	Dominant Responses	
		Back	Other Part
Back-FACE.....	74	19	55
Back-GENITALS.....	62	23	39
Back-SHOULDER.....	84	29	55
Back-BUTTOCK.....	76	27	49
Back-foot.....	66	35	31
Back-BREAST.....	64	22	42
BACK thigh.....	77	49	28
Back-abdomen.....	61	27	34
BACK-hand.....	85	70	15
Thigh Combinations	Total Errors	Dominant Responses	
		Thigh	Other Part
Thigh-FACE.....	47	9	38
Thigh-GENITALS.....	81	16	65
Thigh-SHOULDER.....	59	20	39
Thigh-buttock.....	66	35	31
Thigh-FOOT.....	65	18	47
Thigh-breast.....	50	24	26
Thigh-BACK.....	77	28	49
THIGH-abdomen.....	66	42	24
THIGH-hand.....	76	49	27
Abdomen Combinations	Total Errors	Dominant Responses	
		Abdomen	Other Part
Abdomen-FACE.....	66	15	51
Abdomen-GENITALS.....	81	16	65
Abdomen-SHOULDER.....	74	26	48
Abdomen-BUTTOCK.....	56	16	40
Abdomen-FOOT.....	57	17	40
Abdomen-BREAST.....	64	17	47
Abdomen-back.....	61	34	27
Abdomen-THIGH.....	66	24	42
ABDOMEN-hand.....	86	71	15

\* One hundred tests done in each combination were analyzed statistically. The remaining 20 tests in each combination were of homologous body parts and did not lend themselves to this type of analysis.

† Capital letters indicate dominant part as evidenced by a *t* test value of 5% or less.

In testing normal subjects it was noted that they responded by mentioning the face as being the area touched and only when questioned further did they mention the hand. In other words, there was a preference for the face in the response.

In another series of simultaneous tests of 20 normal adults the following method was used. Twenty normal adults were informed that they were to be touched on two regions of the body and that they were to report only one of the two places stimulated. The eyes were closed during these tests. Ten tests were done in 8 body combinations in a random fashion (tests involving contralateral and homolateral parts of the body) in a manner similar to that used in working out the order of

TABLE 5.—Response on the Initial Trial in Normal Adults Tested in a Single Body Combination

Combination of Body Part		No. of Subjects	Correct	Responses Indicating Dominance of Body Part		Other Responses
A	B			A	B	
FACE*	Hand	160	77	78	5	..
FACE	Breast	94	58	29	2	5
Face	Shoulder	17	9	6	2	0
Face	Penis	30	25	4	1	0
Face	Back	31	22	6	1	2
Face	Foot	30	26	4	0	0
BREAST	Hand	76	40	31	3	2
Shoulder	Hand	30	24	2	2	2
Penis	Hand	30	17	11	2	0
Thigh	Hand	30	17	6	7	0
Foot	Hand	54	44	7	2	1
Thigh	Foot	30	16	2	9	3
Breast	Foot	30	23	6	1	0
Shoulder	Breast	32	19	7	4	2
Breast	Thigh	18	9	6	3	0

\* Capital letters indicate dominant part as evidenced by a chi-square value of 5% or less.

TABLE 6.—Simultaneous Touch Stimulations of Various Body Combinations\*

Body Combination	Choices Given		
Face-hand.....	Face 160	Hand 40	
Face-thigh.....	Face 175	Thigh 25	
Face-shoulder.....	Face 142	Shoulder 58	
Face-foot.....	Face 167	Foot 33	
Shoulder-hand.....	Shoulder 158	Hand 42	
Hand-thigh.....	Hand 141	Thigh 59	
Thigh-foot.....	Thigh 108	Foot 97	
Hand-foot.....	Hand 114	Foot 86	

\* There were 200 tests for each combination.

dominance in Groups A and B. There were 200 tests in each combination. The genital regions were not investigated. The results are recorded in Table 6.

From an analysis of Table 6 it is obvious that the face is the part of the body which is chosen oftenest when it and other parts of the body are touched simultaneously. These findings support the results obtained by other methods. However, this method of selection, when the subject knows that two parts of the body are being touched, did not reveal the expected hand inferiority. This finding does not necessarily detract from observations obtained by the methods described above, where the subject was to report what he perceived after he was touched in two places without warning.

After this series of tests each of these 20 subjects was asked to indicate which part of the body they were the most and the least aware of during testing. The results are tabulated in Table 7.

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Of significance in both sets of these experiments is the fact that the face shows a high dominance. However, it must be stressed again that the last two methods do not reflect the low order of hand dominance.

4. *Adults with Schizophrenia.*—When these patients made errors, the errors were similar to those obtained in normal adults under the age of 65. Each patient showed significant dominance of the face to the hand as well as to the foot, the breast to the hand and foot, and the penis to the hand and foot (Table 8).

The relationship of all the body areas has not been worked out so completely in these subjects as in the preceding groups. The difficulty in demonstrating the

TABLE 7.—*Responses of Twenty Patients as to Areas of Greatest and Least Dominance*

Body Part Most Aware of	No. of Subjects	Body Part Least Aware of	No. of Subjects
Face .....	10	Thigh .....	10
Face and foot.....	1	Foot .....	4
Face and thigh.....	1	Hand .....	3
Hand .....	1	Shoulder and thigh.....	1
Foot .....	1	Foot and shoulder.....	1
		Not asked.....	1

TABLE 8.—*Response on the Initial Trial in Schizophrenic Adults Tested in a Single Body Combination*

Combination of Body Part		No. of Subjects	Correct	Responses Indicating Dominance of Body Part		Other Responses
A	B			A	B	
FACE *	Hand	72	24	46	2	..
Face	Breast	81	52	14	11	4
Face	Penis	30	23	3	2	2
Face	Back	42	29	7	4	2
FACE	Foot	37	25	12	0	0
Face	Shoulder	13	2	8	3	0
Shoulder	Hand	31	19	8	3	1
BREAST	Hand	77	29	44	1	3
PENIS	Hand	43	20	19	3	1
Thigh	Hand	30	9	11	9	1
Foot	Hand	31	15	8	6	2
Thigh	Foot	30	15	4	10	1
BREAST	Foot	30	9	19	1	1
PENIS	Foot	30	17	8	2	3
Shoulder	Breast	28	15	3	8	2

\* Capital letters indicate dominant part as evidenced by a chi-square value of 5% or less.

complete pattern in schizophrenic patients was the same as that encountered in normal adults. They showed fewer perceptual errors on simultaneous tests than did either patients with organic brain disease or children. These errors occurred only during the initial trials, so that one subject could be tested for only one body combination.‡

‡ There were a number of patients with schizophrenia who presented bizarre responses. The touch stimuli were occasionally misidentified and were reported as "a burning" or "a fly crawling." At times the number of percepts were multiplied. Instead of perceiving the two applied stimuli, they reported three or more percepts in a variety of body parts. Similarly, a single stimulus was reported as two or more percepts, the locus of the original stimulus being occasionally omitted. Such patients usually persisted in the bizarre responses on repeated testing on subsequent days. Several of the paranoid patients refused to close their eyes but permitted examination provided they could see.



5. *Senile Adults*.—Studies of body combination tests in senile adults 65 to 96 years of age showed results similar to those found in patients with disease of the brain and in very young children.<sup>4</sup> The most dominant region was the face and the least dominant the hand. In plotting the errors on face-hand tests in normal subjects of all ages, we found that children under the age of 6 years and adults over the age of 65 show the greatest incidence.

6. *Supplementary Studies of Blind or Deaf Subjects*.—While we were conducting the foregoing experiments, we, naturally, tried to find an explanation for face dominance. One of the thoughts we entertained was that normal subjects developed the concept of the face being foremost in importance. It might be assumed that the earliest sensory image a subject experiences would be the sight of the mother during infancy. Therefore, the earliest memory of a person and his self-identification would be the visual image of a face. Moreover, young children who are asked to draw the picture of a man draw the face first and foremost, paying less attention to other parts of the body. Goodenough<sup>15</sup> made similar observations on the drawings of mentally retarded persons and patients with disease of the brain. Since visual memory and imagery of a face would seem to be important in one's sensory experience, it was thought that the congenitally blind might not respond as the normal subject does when he is tested with cutaneous stimulations. With this in mind, a series of congenitally blind children and another series of adults with an organic mental syndrome and long-standing acquired blindness were tested with double simultaneous stimulation of the face and hand. Results showed that there was no difference in the pattern of response between the blind and the normal subjects.

A. Blind Subjects: I. Children. Forty-two normal children (3 to 14 years of age) with congenital blindness were tested in face-hand and hand-foot combinations. Ten tests (heterologous and homolateral parts of the body) were done for each combination in a random order.

The results obtained were as follows:

1. Of all children 6 years of age or younger who were congenitally blind, 79% showed persistent errors after 10 trials of testing.

2. In the face-hand combination tests the following responses were obtained:

Face Only	Face-Face	Hand Only	Hand-Hand
202	34	2	1

3. In the foot-hand combination tests the responses were as follows:

Foot Only	Foot-Foot and Partial Displacement of Hand Stimulus	Hand Only	Hand-Hand
51	26	26	9

4. The pattern of all errors throughout the testing was the same as that for normal children without blindness.

II. Adults. Ten adults with an organic mental syndrome and blindness acquired after childhood were tested with multiple face-hand tests. All showed persistent errors. The analysis of all the errors are as follows:

Face Only	Face-Face	Hand Only	Hand-Hand
100	7	1	1

From this analysis it is obvious that preservation of vision in infancy is not essential for face dominance.

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B. Deaf Subjects: We also thought of other causes for face dominance, namely, that the touch applied to the face was not only felt but reinforced by the sound stimulus produced by the touch on the face, which is so near the ear. To establish or exclude this possibility, we studied a series of deaf people.

Thirty-two adults with deafness acquired in early infancy or childhood were tested with multiple face-hand tests. These subjects were otherwise normal. They had no evidence of disease of the brain. The results are indicated in Table 9.

Again we found face dominance. Hearing did not seem to be a factor in face dominance.

## COMMENT

From the foregoing studies it is obvious that we have been investigating perceptual functions from the standpoint of patterns. For many years Lashley § has been stressing the fact that the data obtained on neurologic examination should always be analyzed with reference to pattern of activity. We did this in the compilation of our own results. By clinical observation we learned that when the cutaneous sensory field is examined under conditions of simultaneous stimulation a distinct pattern is discerned. The pattern is most apparent in testing two non-

TABLE 9.—Incidence of Errors for Deaf Subjects, Initial and Subsequent Trials

Total No. of Subjects	Initial Trial			
	Correct	Face Only	Face-Face	Hand Only
32	9	19	2	2
	Initial and Subsequent Trials			
	Face Only	Face-Face	Hand Only	Hand-Hand
86	1	4	0	

symmetric regions, far removed from each other and situated along the longitudinal axis of the body. The resultant interaction between these two sensory stimuli yields a characteristic pattern. In studying the data, it was learned that the face is the most dominant region of the organism. The genital zone is next in the order of dominance, while other parts of the body follow in a gradient, with the hand manifesting the least dominance. Thus, the most conspicuous gradient is between the face and the hand. The pattern of response we obtained by testing with the method of double simultaneous stimulation has been found consistently on numerous occasions, under a variety of conditions, and in many groups of subjects.

In considering our results, we naturally ask what the organizing principle of this perceptual pattern might be, or with which neurophysiologic or psychophysiology data it may be correlated. Why is the face the most dominant and the hand the least dominant? Why does the genital region show a high dominance? What determines such an order of dominance? Is it acquired by learning; is it inherent, or is it a product of each? If it is inherent, what role does the body image play?

*Anatomic or Neuro-"Electrical" Studies.*—In considering the anatomic substrate, we find no apparent correlation of findings elicited on electrical studies of the cerebral cortex with areas of the body which show dominance by our method of stimulation. Some aspects of tactile sensory interaction have been discussed by

§ References 16 through 18.

Marshall, Woolsey, and Bard<sup>19</sup> in their mappings of the cerebral cortex of the cat and monkey by the method of evoked action potentials. The map of the "sensory cortex" as determined by electrical stimulation or evoked action potentials does not serve to explain the order of dominance. It might be supposed that the degree of dominance found in a part of the body would be proportioned to the area in the cerebral cortex in which this part of the body is electrically represented. However, this is not the case. The face and the hand, the most and the least dominant areas, respectively, in our system of testing, have approximately equal representation in the homunculus of the human cortex as determined by the method of electric stimulation of the cerebrum.<sup>20</sup>

It is not certain whether electrical studies on neuron action will give us the answer, for, as Lashley has repeatedly pointed out, most studies are made on surgically isolated or anesthetized animals, and these are far from being in a physiologic state. Our own clinical studies show patterning of sensory interaction in the physiologic state of man, whether there is or is no disease of the brain. This is a physiologic fact. The meaning of this fact, however, is not as yet clear. This patterning of sensory interaction does not occur in any one region of the cortex. It is the result of integration of perceptual function, which takes place in the entire brain at the cortical, thalamic, and even lower levels of the nervous system. There is no doubt that sensory interaction occurs, but that this interaction is patterned and how it is patterned is still a mystery.

*Psychophysiologic Studies.*—Our own psychophysiologic data also fail to shed any light on our problem. Studies of thresholds of cutaneous sensations, types and nature of stimuli, and attention of subject and sensorimotor responses did not offer clues to a solution. Critchley,<sup>21</sup> in his interesting article on tactile functions in the blind, suggested that face dominance may be due to the sensitivity of the skin. It does not seem to be a matter of thresholds,<sup>22</sup> for we have been working with crude supraliminal stimulations. The stimuli we employed consisted for the most part of firm taps or scratching and slapping of the face and hand, or repetitive or moving stimulations, such as rubbing. Moreover, the tactile thresholds, as obtained in different regions of the cutaneous sensory field by use of the method of von Frey,<sup>23</sup> using von Frey's hairs (Table 10), or with a stimulus such as pinprick (Table 11), show no strict correspondence to the "dominance" values obtained by the method of simultaneous tactile or pinprick stimulations. The use of stronger or more noxious stimuli, such as pinpricks, will reveal a lower incidence of errors, but the pattern of dominance will be the same.

Nor is there any correlation between the acuity of the sense of two-point discrimination and the order of dominance. It will be recalled that the ability to discriminate two points at the finger tips or at the hand is much greater than that at many other parts of the body, excluding the lips and tongue; yet the hand shows the lowest order of dominance. This lack of correspondence is contrary to the hypothesis proposed by Denny-Brown, Meyer, and Horenstein, who studied patients with lesions of the parietal lobe.<sup>24</sup> In our studies of normal subjects and of patients with disease of the brain, including that of the parietal lobe, we find no correlation between incidence of errors as elicited by the method of double simultaneous stimulation and the two-point discriminative potentialities of a given cutaneous area.

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Still another factor to consider is that of attention. Critchley,<sup>||</sup> in a series of papers, claims that it is a lack of attention which causes the imperception of one of the two simultaneous stimuli in patients with lesions of the parietal lobe. As expected, this type of sensory defect is apparent only on the side opposite the cerebral lesion. It is especially pronounced in the hand and least manifest in the face, thus reflecting a pattern with an order of dominance similar to the one illustrated in normal children and in subjects with diffuse disease of the brain. If this pattern in the parietal lobe lesion is interpreted as due to a lack of atten-

TABLE 10.—*Stimulus Threshold for Pressure, in Grams per Square Millimeter, After von Frey*

Cornea .....	0.3	Hand, dorsum .....	12
Conjunctiva .....	2.0	Foot, dorsum .....	15
Tongue .....	2.0	Calf .....	16
Nose .....	2.0	Prepuce .....	16
Lip .....	2.5	Spinous processes .....	16
Finger tip .....	3.0	Medial edge of scapula .....	16
Eyelid (edge) .....	3.0	Deltoid muscle .....	17
Infraorbital area .....	3.0	Upper arm, extensor surface .....	26
Forehead .....	3.0	Abdomen .....	26
Hollow of palm .....	7	Orifice of urethra .....	26
Dorsum of fingers .....	5.0	Thigh, outer side .....	27
Upper arm, flexor surface .....	7	Areola of breast .....	27
Thigh, inner side .....	7	Undersurface of breast .....	27
Forearm, flexor surface .....	8	Sole, noncalloused part .....	28
Nipple .....	8	Tibia .....	28
Anterior edge of deltoid .....	9	Forearm, extensor surface .....	33
Anterior edge of axilla .....	11	Inguinal area .....	48
Xyphoid process .....	11	Glans penis .....	111
Mucosa of cheek .....	12	Sole, calloused part .....	250

TABLE 11.—*Stimulus Threshold for Pain, in Grams per Square Millimeter, After von Frey*

Cornea .....	0.2	Upper thigh	
Conjunctiva .....	2	Outer surface .....	30
Eyelid .....	10	Inner surface .....	30
Abdomen .....	15	Extensor surface .....	40
Forearm		Foot, dorsum .....	50
Flexor surface .....	30	Hand, dorsum .....	100
Extensor surface .....	30	Tibia .....	100
Upper arm		Internal malleolus .....	110
Flexor surface .....	30	Hand, palm .....	130
Outer condyle of humerus .....	30	Sole, calloused portion .....	200
Cheek .....	30	Finger tip .....	300
Calf .....	30		

tion, it must be that the inattention is only on one side of the body, and particularly in the hand. In other words, the term inattention becomes synonymous with defective perception produced by the parietal lobe lesion.

Nevertheless, attention tends to modify perceptual responses. According to William James, "when the things to be attended are small sensations and when the effort is to be exact in noting them it is found that attention to one interferes a good deal with the perception of the other."<sup>46</sup> But does this explain the pattern in dominance or in errors in perception as illustrated in Figures 1 and 2? It might be claimed that man pays most attention to the face because he is most interested

<sup>||</sup> References 25 through 28.

in this part of the body. Such reasoning may explain face dominance, but it does not account for the frequent errors made in the hand stimulus. The latter finding would imply that man pays the least attention to the hand, less than to any other part of the body. Now, it is hardly likely that one pays less attention to one's hands than to one's back. Yet, according to our data, the back dominates over the hand, implying that man is more interested in his back than in his hand. This is contradictory, and it becomes obvious that attention does not account for the order of dominance as depicted in Figures 1 and 2. A defect in attention may crystallize but not determine the pattern of perception as elicited by the method of double simultaneous stimulation. Further evidence against the attention theory are the recent experiments by Hooker.<sup>29</sup> He found an order of dominance in sensation, using double simultaneous touch stimulations, in the human fetus. Even though the response to stimuli in his experiments involves an order lower than that implied in our results, there was a distinct pattern under his conditions of testing in which attention was not a factor. When there was simultaneous cutaneous stimulation of the face and hand, the dominant motor response was that typical of the face.

An important principle to consider in the study of patterns of response to sensory stimuli is that every sensation has a motor component. Thus, when we request the subject to report what is felt when the face and hand are touched simultaneously, there must be an efferent, or a motor, element. The patient replies verbally and tends to point to the spots touched. In a series of face-hand combination tests or in combinations involving the face and another body part, it was shown that the face is the first to be indicated, whether it is pointed to with the hand or announced verbally (Table 6). Since the hand is used in the pointing, it would be the last of the two (face and hand) perceived regions to which the subject would point. On the contrary, the face would be the first to be indicated. This, however, is not always the case, for when both stimuli are perceived, the hand is sometimes the first to be indicated. This is particularly evident in combinations which do not include the face. When both hands are stimulated, the incidence of errors is very low and the subject often uses either hand to point to the other.

*Learned and Inherent Perceptual Organization.*—Perceptual organization or sensory correlation may proceed along two lines: (1) learning or individual acquisition of perceptions and (2) inherited or genetically determined perceptual patterns. Acquired perceptions are organized in the course of experience by the postulated mechanisms of pattern identification, by a selective process, by symbolization, and by conceptual organization. As Nissen states, "Symbolization helps in perceptual organization also in connecting percepts with concepts to specific responses."<sup>30</sup>

1. *Learning Factor:* There are many who believe that all perceptions and perceptual patterns are acquired. Most perceptual reactions are learned during the maturation period or infancy. In our own studies of perceptual patterns under conditions of double simultaneous stimulation, we believe that awareness of the part of the body, such as the genital region, is an example of learning. Infants or children learn of and become aware of their genitals. Initially, when the pattern was demonstrated in adults with disease of the brain, the high dominance manifested in the genital region was not too surprising. The interpretation was that, due to its special sexual connotation acquired by learning, there is more "awareness" of

stimuli applied in this area. The question then arose as to what the pattern would be in very young children. If sexual "awareness" was not yet operative, that is, if the child had not yet learned of the social significance of the genital organs, one might assume that there might be less dominance of the genital zone than in adults. However, in our studies we found that young children were indeed "sensitive" about their genitals. Most of the children under 6 years of age, even the very youngest, who were just about able to cooperate in the perceptual tests, were reluctant to expose this area or showed some form of embarrassment or curiosity when their genitals were touched. Some refused to have more than a few tests done at one time. Evidently this increased "awareness" is learned prior to 3 years of age. Since we found a high dominance for the genital area in children, it might be inferred that this high dominance is related to a sexual awareness which was probably learned in the first two to three years of life.

Schilder ¶ pointed this out in his discussion of the principles concerning the libidinous structure of "the body image." # He stated:

The attitude toward the different parts of the body can be determined by the interest the persons around us give to our body. We elaborate our body image according to the experiences we obtain through the actions and attitudes of others. The actions of others may provoke sensations when they touch and handle us. But they may influence us also by words and actions which direct our attention to particular parts of their body and our own body. . . . Early infantile experiences are of special importance in this connection but we never cease gathering experiences and exploring our own body.<sup>31</sup>

These principles of symbolization in perceptual organization apply to genital as well as to other regions of the body. From the psychoanalytic, or Freudian, point of view the face and the mouth participate in the oral stage of body image, or, more correctly, of body schema development. The same school emphasizes that the genital region plays a great role in the development of the organism. Therefore, it should not be surprising to find the face and genital regions almost on the same level of dominance as determined by double simultaneous stimulation.

¶ References 31 and 32.

# Smythies,<sup>33</sup> in a philosophical paper, criticized the confusion and the loose use of the term "body image." Thus, (a) there is "the body image" which describes "a visual, mental, or memory image of a human body, one's own or someone else's." Body images are experienced. (b) Body schema should be used only in its original sense. It is part of the subconscious mind, and thus its presence is inferred, and not experienced. The experiments of Stratton are a good example of almost a pure disorder of the body schema. (c) Body concept is a conceptual constellation and depends largely upon the proper function of the relevant memory mechanisms. Anosognosia is an example of disorder of the body concept. (d) "The perceived body," or another name for it, "postural model of the body," a term to be applied to the somatic sensory field—directly experienced inside central consciousness. An example of this is the experience of having a phantom limb or autotopagnosia. The perceived body is identifiable with the "body image in the brain." (e) Actual physical body is a physical object and not the same as the perceived body. What one perceives as to body parts does not always correspond to the actual position of the physical body and vice versa. An example of this is found in the patient's experiences in mescaline intoxication, where the perceived body is not the same as the physical body. Also the postures assumed in some of the dyskinesias are not always perceived. (f) Body image in the brain of the physical body (theory of psychoneural identity). The homunculus as determined by electrical stimulation or destruction of brain tissues is an example.

While we agree with Smythies criticisms, it is sometimes extremely difficult to use his classification of "experiences and description of the human body." Nevertheless, in our subsequent discussions we shall try to use his terms wherever possible.



Even though Schilder\* proposed these theories, there are no clear-cut experiments to show that the face is sensitized the most, and, for that matter, that the hand is sensitized the least, in the maturation of the normal infant or child. As a matter of fact, in the same book Schilder emphasized the importance of other structures in the construction of the "body image." In considering "sexual sensitization" of body parts in adults, one must compare such erogenous zones as the breast and buttock with the genital region. Yet analysis of our data reveals no undue dominance of the breast and buttock over nonerogenous regions, such as the foot or abdomen. Perhaps there would be no incongruity in dominance of erogenous zones if we interpreted our data from the standpoint of age, sex, personality, and social background of the subject. Under such conditions we might have found different gradients in each group and concluded that sensitizations of the body parts by learning are, after all, important, but not necessarily the principal factor in determination of the pattern.

In this connection the question of the development of the "body image" arises. How does the "body image" develop? Schilder admits that we have no reliable information as to how this development takes place. He said that there is "reason to believe that there is an inner development, maturation, . . . and there are inner factors, which are given in the organism and comparatively independent of experience which determines this development." He also believed that "the process of maturation gets its final shape through individual experience." Thus, there is a factor of maturation which forms the basic structure of the body image, whereas experience and learning influence the trends of the development. Maturation and learning are essential features of all types of development, whether it is body image, body schema, body concept, perceived body, or perception itself. These conclusions are partly supported by the experiments of Gesell.<sup>34</sup>

If this sort of reasoning, namely, development of the body image in infancy, accounts for face-genital dominance, what explains the inferiority of the hand, as determined by this series of tests? When the hand is considered in the spectrum of the "body image," there seems to be no prominent reason for its inferior position. According to Schilder, the hand is an important structure in the formation of the "body image." The "body image" is continuously influenced by the almost constant optic image of its hands. One sees his own hands more frequently than any other part of his own body. In fact, perceptually and from the motor standpoint the hand is one of the most important structures in the "perceived body." Katz<sup>35</sup> says that the hand makes the most vivid impression. Despite this, it is curious that the hand is least dominant when it is tested simultaneously with another body part.

2. Inherent Factor: Thus far we have discussed the factor of learning in perception as the basis for the pattern we obtained on double simultaneous stimulation. It is possible that "learning" during infancy might explain part of, but not the entire, pattern of sensory organization under conditions of double simultaneous stimulation. However, our results show that the factor of "learning" did not enter in our own tests. An analysis of the responses obtained on the first trial in many children showed that the face was most dominant and the hand was least dominant. In this situation there was no opportunity for learning; yet this pattern was found on the initial tests in most subjects. The same consistent initial response was obtained

\* References 31 and 32.

in tests of combinations of other body regions, such as the hand and the thigh, etc. These findings strongly suggest that the patterns we obtained are not the result of a learning process during testing but may be due to inherent sensory organization. This theory is supported by the preliminary studies of Hooker.<sup>29</sup> Working with human fetuses, he found that double tactile simultaneous stimulation of the face and hand resulted only in the face reactions. When the hand and foot were tested, there was only the hand response. Thus, there was an order of dominance in which the face dominated over the hand and the hand over the foot. Although the pattern Hooker obtained in the fetus is not exactly the same as the one we obtained under our conditions of double simultaneous stimulation in young children, the fact remains that a pattern has been observed before the organism had an opportunity to learn. Carmichael,<sup>30</sup> after reviewing the available experimental data, concludes that there is only little evidence that learning modifies fetal behavior. If it is assumed that the pattern is determined inherently, one should consider the role the body image plays in organization of perception or in the order of perceptual dominance.

3. Organization of Perception in the Perceived Body, Body Image, and Body Concept: (a) Perceived body. In a discussion of the inherent properties of perception we must consider the role of the "perceived body." There is a theory that midline structures of the body dominate over the lateral or peripheral parts. In his monograph on the body image, Schilder emphasized the dominance of the midline structures. This theory considers the long axis of the body as being the dominant over other regions. Part of the same theory is that proximal parts of a limb dominate over distal regions. In our own experiments it is true that the face and the genital region, both midline or axial regions, are the most dominant parts of the perceived body. However, this axial theory does not account for the gradients as depicted in the graph we plotted from our data. There are some midline or axial structures which show no significant dominance over the lateral parts. Thus, the foot, a lateral area, is dominant or equal to the thigh, which is a proximal area, and to the buttock, which is an axial structure. Moreover, there is a differentiation of dominance along the longitudinal axis of the body itself. Thus, the face or the genital region is dominant over the abdomen, buttock, or midback.

A second hypothesis is the one proposed by Cohn.<sup>37</sup> This is similar to the first. Cohn proposed that the pattern of dominance, as elicited by the method of double simultaneous stimulation, is inherently organized on the basis of rostral dominance, i. e., the theory that the face is the most dominant part of the organism, while the remaining body areas show a descending gradient along the longitudinal axis. The rostral parts are dominant over the more caudal areas. This theory is consistent with the extensive observations on the development of the vertebrate nervous system, in which a rostral-caudal gradient is demonstrated in phylogenesis.<sup>38</sup> This gradient is manifest in the progressive differentiation of the rostrum until, in Mammalia, the cerebrum is fully differentiated. The gradient is also manifest in biochemical and physiologic reactions at each phylogenetic level. Similar gradients have been demonstrated for the musculoskeletal and gastrointestinal systems. A rostrocaudal order of sensory development has also been shown to exist in ontogenesis in studies of the fetus with single stimulations.<sup>39</sup> More recently, Hooker<sup>29</sup> found such an order in human fetuses when the face and hand, or hand and foot, were touched simultaneously. Our own data support this theory of rostrality only in part, inasmuch as there is face dominance. However, other facts tend to contra-

dict the theory of rostrality. There is no continuous downward gradient between the rostral and the caudal region. Even though the face is most dominant, there are caudal body parts which are dominant over some of the more rostral regions. For example, the foot is dominant to the hand and the thigh. Most significant is the dominance of the genital region to all more rostral areas except the face. From the foregoing data one must conclude that the concept of rostrocaudal order of sensory organization is not applicable beyond the fetal stage. There may be the factor of learning and maturity in the postnatal stage. More studies of double simultaneous stimulation in different parts of the body of the human fetus, particularly the genital region, may shed more light. Similar studies in the first year of life will help us in understanding the development and organization of perception in man.<sup>40</sup>

(b) Body image and body concept. Another theory can be evolved in considering the relation of the body to its inner self or that of the ego to its outer world. This concept implies that the ego has a center and a periphery region, just as the perceived body has an inside and an outside. We observe ourselves (inside) as we observe others (outside). When one thinks of himself, what Schilder called *autoscopy*,<sup>42</sup> there is an image of one's own face. This is a good example of what is meant by body image. Children in making drawings of a man indicate the face, while other parts of the body are less often illustrated.<sup>18</sup> Even congenitally blind children, in whom the hands and fingers are of especial importance, model the head as being too large<sup>41</sup> and the region of the mouth as being the most conspicuous.†

In expressing the concept of the ego in terms of body parts, the face is visualized or comes to the foreground more than any other structure. The face is the most distinguishing part of the organism itself. The face represents the most central or inner portion of the ego. In narcissism the self-interest in one's body is directed chiefly to the face. Claparède,<sup>43</sup> in his studies on localization of the self, concluded that the ego is conceived as being in the head. More specifically, he believed the center of the ego is situated between the eyes. As for the genital region, there are many, particularly the psychoanalysts, who would identify this area of the body with the inner part of the ego.

The part of the body which has to do with reproduction is probably just as "deeply in" or central in the organism's concept of the body as is the head, with its face, mouth, eyes, etc. In considering the genital region, it is not always easy to determine whether the importance attached to this part of the body is due to inherent or to acquired factors. There is a great deal of literature on this subject, but it is still difficult to ascertain what role the inherent factor plays as opposed to the learning factor.

Applying the theory of centrality, i. e., that the face-genital regions are innermost in the ego and in the body concept, we are faced with the problem of fitting the hand into this theory. In contrast to the concept of the face or genitals being central, the hand is mostly on the periphery. The hand is the medium with which we or our ego makes contact with the peripheral or outside world. The hand is on the periphery of our ego structure and, with the aid of vision, is the most important tool for exploration of the outer world. One might argue that the foot, although a distal structure, also makes contact with the outer world. However, in this task the

† von Stockert, F.: Quoted by Critchley.<sup>21</sup>

hand, in most instances, is used more than the foot. Moreover, the impression gained is that the foot is more inward—it seems more protected and hidden by shoes. In summary, it would appear that from the standpoint of body concept organization within the ego, the face and the genitals are the most inwardly situated, while the hand is least centrally or most peripherally situated in the conceptual organization of body parts within the ego. Now if we correlate the latter hypothetical pattern with the pattern we found in our perceptual tests, we create some sort of congruity between the two, namely, (a) face dominance as obtained on perceptual tests with face as the most inner portion of the ego, and (b) hand inferiority with hand as the most peripheral portion of the ego. From this it might be inferred that the ego may play a role in the determination of the perceptual pattern. We realize that this is a highly theoretical explanation. Obviously, the concept of the hand being the most distal, and the face the most central, portion in the organization of perception in body image needs testing. We also realize that our results may be colored by an obscure artifact, although we have checked our data by a variety of methods and conditions of testing.

If this concept is at all valid, it should be applicable to functions other than those of cutaneous senses. Thus, the concept of "central" portions dominating over the periphery may be found in studies of vision. Observations drawn from patients with mental changes consequent to diffuse brain disease show domination of central over peripheral vision. Goldstein<sup>‡</sup> and others have found that in these patients constricted fields of vision are not uncommon. When such a patient is instructed to fix at a central target and report whether he sees another target simultaneously in the periphery of the field, the response is that the central target is observed and not the one in the periphery.<sup>48</sup>

In studies of visual responses of these patients to rapid exposures of images with groups of figures, it was noted that they reported what they saw in the central portion of the field only, often not observing the peripheral figures. Similar results were obtained in tachistoscopic examinations of mentally defective persons. In all these cases the results were uniform, namely, the perception of the central, but not of the peripheral, figures. Thus, when the cutaneous sensory field is compared with the visuosensory field, the face seems to correspond to the macular region, and the hand, to the most peripheral part of the field of vision. On further comparison, it might be inferred that central vision is identifiable with the ego in the same manner as is the face. The optic image we have of ourselves or of others is situated in the central portion of the field of vision. Our ego is projected in the central regions of the perceptual field. In considering these patterns for perceptual function, we touched on the topic of conceptual functions. When the subject of the ego is discussed, a pattern for thinking becomes obvious. It is well known that most of our thoughts are pointed directly or indirectly toward ourselves, and we think least of what is most peripheral to or away from the ego. This subject has been amply discussed by William James in his "Principles of Psychology." The object of mentioning the parallel was to point out the principle that similar patterns exist in all types of perceptual functions, as well as in conceptual and motor functions.

<sup>‡</sup> References 43 and 44.

SUMMARY

Tests of simultaneous tactile stimulation involving many different body combinations were applied to patients with an organic mental syndrome, normal children, normal adults, and schizophrenic adults. By the use of these simultaneous touch stimuli, a pattern in cutaneous perception was demonstrated in which the face, as well as the genital region, was the most perceptive or dominant body area, whereas the hand showed the least dominance. The remainder of the body regions fell between these two extremes in the form of a mild gradient. No one theory adequately explains the organization of this pattern. Learning and maturation are probably factors, but it appears to be mostly inherent. The pattern is found in the normal subject but is accentuated in the presence of disease of the brain.

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## Society Transactions

### CHICAGO NEUROLOGICAL SOCIETY

Douglas N. Buchanan, M.D., *President*

Leo A. Kaplan, M.D., *Secretary*†

*Regular Meeting, Jan. 12, 1954*

**Hemispherectomy in Infantile Hemiplegia.** DR. M. A. PERLSTEIN (by invitation) and DR. OSCAR SUGAR.

This presentation consists of two case reports on children, one with a right hemiplegia and one with a left hemiplegia; both children had convulsions primarily of a focal nature which did not respond to intensive drug therapy. In both cases marked improvement followed the surgical procedure. Convulsions were controlled and behavior improved. In the second boy there was a gain in mental age of 10 months in the two months following the hemispherectomy.

As can be expected, both children have hemianopsia and both still have their hemiplegia, although the function of the involved arm is markedly improved. From the point of view of the perceptual testing no change was noted qualitatively, although there was an increased speed in performing tasks.

The clinical results in these two cases would indicate that the neurosurgical procedure of hemispherectomy can be done safely and with markedly beneficial results in selected patients with hemiplegia who are not responding to drug and other forms of therapy.

#### DISCUSSION

MR. JOHN HANKINSON, London, England: My chief in London has performed hemispherectomy for infantile hemiplegia and for behavior disorders on 30 occasions. The operative mortality has been nil. We lost one child at the end of three months from low-grade meningitis. These cases have been carefully selected by the personnel at Queen Square from a very large number of children suffering from these disorders. Dr. E. A. Carmichael, a neurologist, Mr. Wylie McKissok, a neurosurgeon, and a radiologist consider these cases. The first 18 of these cases were reported at the Royal Society of Medicine in October, 1953. These cases correspond very considerably with the cases just presented in the striking incidence of behavior disturbances and also in the subsequent lack of seizures and improvement in behavior. Of these first 18 patients, 15 have had no further convulsions in a long follow-up, one to three years. A small number are very greatly improved as to behavior; now they are lovable, where before their behavior was almost impossible. The youngest was 18 months; the oldest, 22 years.

My only other comment is in regard to movement of the hands, which was remarked upon here. At the end of this operation, if the patient is in good condition, he can initiate movements in both lower limbs, which have been demonstrated in a movie (*Brain* 76:405, 1953).

One more point, in most of these cases hypotension has been induced with hexamethonium. This is induced just before amputation of the hemisphere is undertaken. The preliminary surgery and investigation were done with the patient under light anesthesia. We always remove the choroid plexus because in the earlier case we got secondary hydrocephalus from leaving the choroid plexus.

DR. FREDERIC A. GIBBS: Dr. Perlstein's wonderfully lucid presentation included all the significant electroencephalographic data on these cases, and I can add nothing.

DR. I. JOSHUA SPIEGEL: I should be interested in hearing a few details of the actual surgical procedure.

† Dr. Leo A. Kaplan died Feb. 20, 1954.

DR. OSCAR SUGAR: A large craniotomy is done. In the infantile hemisphere, as you well know, the vault is smaller on the side of the smaller hemisphere, and therefore it is relatively important to make sure that the saw is not passed on the wrong side of the midline and enter the longitudinal sinus. Such a slip can be disastrous.

The case that was presented here had cysts in the temporo-occipital region; these cysts communicated neither with the subarachnoid space nor with the large ventricle. The electroencephalogram taken at the time of operation showed independent spiking on the part of the left frontal lobe having to do with speech. It was with some trepidation that I decided that that part of the brain had to be excised. In communication with Dr. J. M. Nielsen, on the West Coast, I learned that if the speech center is damaged before the age of 10, the child will recover his speech. In one of the earlier hemispherectomies I did, in which the patient, unfortunately, died of hydrocephalus, I did not take out the choroid plexus. I do now. I took that hemisphere out in one piece. Dr. A. Earl Walker does his hemispherectomy by taking out the block in one piece. It is easier to take the tissue out in two pieces, removing the frontal lobe by itself. You do not clip the middle cerebral artery at the point where it leaves the internal carotid artery. It is caught over the island and clipped there. The anterior cerebral artery is caught between the two hemispheres. The first incision is across the distal portion of the frontal lobe; then it is easy to take out the rest. The corpus callosum is opened, and the basal nuclei come away from the cerebral cortex. The operation is not really difficult, especially if you have plenty of help to give intravenous fluid and blood transfusions in a hurry, if need be.

**An Unusual Case of Extradural Hemorrhage.** DR. PETER V. WESTHAYSEN (by invitation) and DR. HAROLD C. VORIS.

We are reporting a case of extradural hemorrhage with some unusual features.

The patient, a 23-year-old white man, complained of progressively severe headache for five days and gave a history of a trivial antecedent head injury. He had a partial right frontal lobectomy and tantalum cranioplasty two years before for extensive frontal lobe scar, producing uncontrollable seizures, which resulted from severe intracranial suppuration eight years before. The only significant findings on admission were, first, bloody spinal fluid and, later, xanthochromic spinal fluid with scalp edema developing over the plate in the right frontal region. At operation a large intracranial hemorrhage was found, which, as a result of the complete lack of regeneration of the previously defective dura, filled the right anterior fossa and became intraventricular because of a porencephalic communication of the lateral ventricle with the intracranial cavity. The hemorrhage was thought to arise from extradural veins. The absence of dural regeneration is in our experience very unusual.

DISCUSSION

DR. HAROLD C. VORIS: In my experience with extradural hemorrhage this case is unique from several standpoints. First, as Dr. Westhaysen pointed out, the antecedent injury was mild and insignificant. This hemorrhage appears to be associated with this relatively mild antecedent trauma; this relation is more characteristic, of course, of a subdural hemorrhage than of an extradural hemorrhage, with which there is usually a severer antecedent trauma. Even more remarkable, as Dr. Westhaysen said, is the complete failure of regeneration of the dura, which usually regenerates very well even when it has been resected over a wide area. The occurrence of extradural hemorrhage in the presence of a dural defect and this peculiar membrane with a stoma made possible the accumulation of a large amount of blood in the cranial fossa without more clinical signs than the patient presented.

**The Metabolism of Convulsions.** DR. L. G. AROOD (by invitation), DR. JAMES BAIN (by invitation), DR. ALEXANDER GEIGER (by invitation), and DR. R. W. GERARD.

The general view on the metabolism of convulsions is as follows: Some sort of excitation of the relevant neurones occurs (and in the case of acridone convulsions appear when the drug concentration in the cat cortex reaches 15 to 20 mg. per gram, whether applied locally or given intravenously); the increased activity demands added energy; this is supplied initially by splitting the energy-rich phosphate esters, creatinephosphate (CrP) and adenosinetriphosphate

(ATP); energy is later contributed by the glycolysis of extra glucose to lactic acid; finally, an increase in oxygen consumption and burning of glucose reestablishes the initial resting state. Our findings indicate that the fall in phosphate esters is due to decreased formation rather than to increased breakdown, that carbohydrate need not, and perhaps cannot, be the fuel, and that convulsive activity can continue even when accompanied by a decrease in oxygen and glucose use.

On the first point, a decrease in phosphate esters occurs in convulsed brain, tetanized nerve, cathodally polarized muscle, and electrically pulsed brain mitochondria, and a feeble phosphate system is present in the brains of convulsion-prone, but not convulsed, mice. The decreased total is accompanied by a slowed turnover rate (specific activity rise) and must, therefore, be associated with lessened synthesis, and, in the case of mitochondria, the whole effect is due to decoupling coenzyme (DPN) oxidation and phosphate esterification.

The other point is established for the perfused cat brain, with direct chemical measures of influent and effluent, and on brain samples correlated with electrical and motor (head region) evidence of convulsions. During and after convulsions,  $O_2$  consumption is normally increased twofold to fourfold, but in the presence of glutamine or curare it is actually decreased. Glucose entry is greatly decreased during convulsions, and the subsequent increase is not used for oxidation but is accounted for as lactate. Typical convulsive activity and increased oxygen use occur when no carbohydrate is present in perfusion fluid or brain stores. No significant glycogen changes occur, but a considerable increase of nonprotein nitrogen in brain is seen during convulsions and is rapidly lost after them.

These findings indicate the need for drastic reconsideration of current concepts on the role of energy-rich phosphate as an energy source and of glucose as the main fuel of neurone activity.

**Problems of Preventive Psychiatry in Korea.** DR. DAVID MCK. RIOCH (by invitation), Washington, D. C.

Certain phenomena of acute and subacute situational stress are reviewed for their bearing on preventive psychiatric problems in Civil Defense. Important data are provided in papers on combat psychiatry by Col. Albert Glass, M.C., U. S. A., and his former associates in Korea. The writings of Brig. Gen. S. L. A. Marshall (Reserve) review a wealth of information from World War II and the Korean war. The chief threat experienced by men under acute situational stress is "loneliness"—that is, isolation, or separation from their organic group, by circumstance or by their own disturbance or failure. Maintenance of communication is of paramount importance but is made increasingly difficult under stress, due to decreased capacity for planning and to constriction of awareness as to both space and time. A clearly defined group mission and an explicit language of minimal complexity to refer to essential functions and places are important supportive measures.

DISCUSSION

DR. LEO A. KAPLAN: Would I be right in concluding that you imply that combat psychiatry resolves itself into the question of returning a man to duty or of evacuating him? What sort of psychiatric treatment is given?

DR. DAVID MCK. RIOCH: From the Division level, after treatment neuropsychiatric casualties may be returned to full duty or to limited duty, or they may be evacuated to Army level. The decisions must be made not only on the condition of the patient but also on the knowledge the Division psychiatrist has of the attitude of the man's unit toward accepting returned neuropsychiatric casualties. This attitude varies from unit to unit. Psychiatric treatment in the combat zone has been described in a number of papers of Col. Albert J. Glass, M.C. In general terms, rest and warm food in a reasonably secure situation are of prime importance. Psychotherapy dealing with the precipitating events and with the immediate emotional needs of the man is used in an effort to reinforce the man's sense of competence and sense of belonging with his unit. In cases of doubt a patient may be held at Division level for a few extra days. From Division level casualties are evacuated to Army level, where they may be treated for two or three weeks. Early treatment, as close to the man's unit as feasible, is desirable to preserve the man's identification with his unit.

DR. BENJAMIN BOSHES: I should like to add our part in the Italian campaign. As Dr. Rioch told his story and showed the pictures, I was moved back 10 years because the terrain was

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almost the same. At the end of 1945 the group in Italy was ordered to prepare a volume for the Surgeon General, which was published as a supplement to the *United States Army Medical Department Bulletin* in November, 1949. That *Bulletin* gives a complete description of psychiatric problems in combat.

I gather that in the early part of 1950 the total United States Army pool comprised two psychiatrists who had real combat experience. One of them was Col. Albert J. Glass. The plan of sending men back quickly to duty was one we adopted in Italy. Colonel Glass started some experimental work on this, and others carried out the policy.

When Col. Fred Hansen was brought back from Italy in 1945, he was placed in G-1, which meant there was some recognition that a psychiatrist belonged close to command. In the meetings of the Neuropsychiatric Society in Italy even General Truscott would come down to one of our monthly sessions. The importance of closer liaison between command and the psychiatrists was proved time and again.

The problems of Korea were like those of World War II, and the solution was through principles worked out chiefly in the Mediterranean Theatre. It is hoped that a sufficient number of combat-wise psychiatrists are available for consultation and planning, should exigencies arise. Principles of civilian psychiatry, while useful, fall short of the needs of the situation when the frame of reference is combat.

DR. DAVID McK. RIOCH: As I mentioned, the methods and organization of military psychiatry in Korea were developed in the African and Italian campaigns of World War II. Col. Albert J. Glass, M.C., largely was personally responsible for establishing the psychiatric service in Korea, and I may note that the success of the service has been due largely to his personal efforts and the personal efforts of his able successor, Col. Donald B. Peterson, M.C. I should like to mention that the better forms of military psychiatry were established very early in the Korean campaign. This is an important item, as there has been a considerable tendency to forget the lessons learned in one war during the interval between wars, with the result that it has been necessary frequently to relearn a great part of the specialty of military medicine during the early phases of a war. Much that had been discovered in World War I was rediscovered during the first year of World War II. It is important that civilian medical organizations support the maintenance and development of the specialty of military medicine during periods of peace.

How close to the line are psychiatrists? One of the main jobs of the Division psychiatrist is to keep in personal contact with Battalion surgeons and with the personnel at Battalion Aid Stations. By visiting the staff during periods of quiet, he can do a great deal both in discussing the recognition and handling of neuropsychiatric casualties and in advising on the utilization of casualties returned to limited duty.

The question was asked as to the problem of neuropsychiatric casualties in Napoleon's armies. I have no information on this question. Presumably men were sacrificed in much the same manner that wounded men were sacrificed, through lack of adequate treatment. I do not think that we are "painting the lily" in our present emphasis on military psychiatry. Although I cannot be specific, I have the impression that the return of a large percentage of neuropsychiatric casualties to duty is an important factor in contributing to what is called "good morale" among the front-line troops.

Douglas N. Buchanan, M.D., President

Leo A. Kaplan, M.D., Secretary

Regular Meeting, Feb. 9, 1954

**An Unusual Case of Paroxysmal Myoclonus.** DR. JOSEPH A. LUHAN and DR. ARCHIBALD McCoy, Joliet, Ill.

The authors presented the case of a 40-year-old housewife suffering from recurrent bouts of rhythmic myoclonus of the proximal thigh and hip girdle musculature, beginning soon after posterior rhizotomy of the 12th thoracic and the first and second lumbar nerves on the right side, performed for intractable pain in the inguinal region of several years' duration. These

paroxysms of shock-like muscular contractions began 11 months before and had been recurring a few days apart. The movements first appeared in the upper lateral thigh musculature of the right side, soon involved the gluteal muscles, and then became associated with feebler, apparently synchronous contractions of similar muscles of the other side. Their frequency was 140 to 144 per minute; they would last for hours, until terminated by intravenous barbiturate sedation or, more recently, by the intravenous use of Solu-B (a mixture of the various B vitamins in powder form for injection after proper solution has been effected) with ascorbic acid, suggestion probably having a potent therapeutic influence in the latter case. The longitudinal history seems consistent with some underlying neurotic predisposition to the patient's present illness. X-ray films disclosed a surgical laminectomy defect of D-12, L-1, and L-2 vertebrae and scattered opacities in various portions of the thoracic and lumbar spine subsequent to a remote myelogram. Spinal fluid studies revealed normal findings. This case was unique in the authors' experience and is provocative of interesting nosological speculation. It is different in a number of ways from Friedreich's case of paramyoclonus multiplex. If one considers this condition a form of neurotic myoclonus, some poorly understood pathophysiological mechanism involving the ventral horn cells must be postulated to explain the nature and situation of the myoclonus, and its paroxysmal nature has an epileptiform connotation.

#### DISCUSSION

DR. R. P. MACKAY: Are these paroxysms always induced by emotion and stress, or are they apparently spontaneous?

DR. JOSEPH A. LUHAN: Those which I observed were apparently spontaneous but were preceded by headache.

DR. OSCAR SUGAR: What about the electroencephalogram?

DR. JOSEPH A. LUHAN: An electroencephalogram was not obtained. For one thing, the facilities for this test were not available in the small hospital where the patient was observed, certainly not at the time the attack was in progress.

However, I did not believe that the origin was in a spreading cerebral cortical epileptiform discharge. The patient had shock-like contractions of part of a muscle, for example, of bilateral mirror-like situation.

DR. BENJAMIN BOSHES: About two years ago I had a case of this type in a man of 60 following an embolus that lasted for four days; the frequency was about 18 per minute, and the myoclonic movements involved the shoulder and arm. They were continuous for four days, even during sleep. The electroencephalogram showed contralateral peaks to a speed of over 100. The man was left with a severe cortical defect, in which the contraction was shock-like.

DR. JOSEPH A. LUHAN: Since I was dealing with a private patient, I was unable to take a movie in slow motion to analyze the movements. The contractions of the gluteus maximus could be reproduced by voluntary innervation, but it was difficult to conceive how a discrete contraction of the upper portion of the quadriceps could be effected through willed movement. If this myoclonus were voluntarily produced, the patient would have to have the endurance of a marathon runner to keep up such a performance, at about 140 contractions per minute for as long as 24 hours in a stretch. This is not the kind of myoclonus or jerking of the limb that we see in myoclonus.

DR. R. P. MACKAY: If this theory is correct, how can one explain the fact that only certain muscles were affected, and how can one explain the sedative effect of vitamin B?

DR. JOSEPH A. LUHAN: I do not know. However, I believe that there was considerable suggestion inherent in the maneuver of administering the medication.

**Surgical Lesions About the Foramen Magnum.** DR. GEORGE S. BAKER, Rochester, Minn.

The abnormal conditions about the foramen magnum which may require neurosurgical procedures for relief of neurologic symptoms are conveniently separated into the congenital lesions and lesions that are acquired after birth. The congenital problems include the anomalies of the

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brain, spinal cord, skull, and upper cervical vertebrae. The commoner conditions placed in this group are Arnold-Chiari malformation, basilar impression, platybasia, spina bifida, meningocele, encephalocele, syringomyelia, gliosis, and arachnoidal adhesions. Tumors, lesions of the vascular system, fractures and dislocations of the upper cervical vertebrae or odontoid process, fibrous dysplasia of bone, osteomalacia, Paget's disease (osteitis deformans), hyperparathyroidism, inflammatory lesions, and acute herniation of the cerebellar lobes through the foramen magnum as a complication of increased intracranial pressure are usually acquired. The neurologic syndromes and the best neurosurgical procedures for relief of symptoms from the author's personal experience were demonstrated by reports of interesting cases and lantern slides.

### DISCUSSION

DR. W. A. GUSTAFSON: We have been interested in this group of frontal lesions for a long time, and in 1939 we presented before this Society a paper on platybasia and malformations (Gustafson, W. A., and Oldberg, E.: Neurologic Significance of Platybasia, *ARCH. NEUROL. & PSYCHIAT.* **44**:1184-1198, 1940). I feel that platybasia, spina bifida, syringomyelia, and arachnoidal adhesions fit into the same category. In platybasia and some of the variables surgical exploration should be carried out.

### Results of Radioactive Isotope Encephalography in Patients with Verified Intracranial Tumors. DR. LOYAL DAVIS and DR. THOMAS CRAIGMILE (by invitation).

Results of isotope encephalography, performed after the administration of radioactive diiodofluorescein or radioactive sodium iodide, in 200 patients with verified primary or metastatic intracranial tumors are reviewed. Primary intracranial tumors were found in 174 cases, while metastatic lesions were encountered in 26 instances.

Analysis of the results in patients with primary tumors reveals a slightly higher incidence of accurate findings following the use of diiodofluorescein—61.6%, as compared with 52.8% after the administration of sodium iodide.

In patients with metastatic intracranial tumors, encephalography following the use of diiodofluorescein produced evidence of the presence of an organic lesion in 76%, while the accuracy rate after administration of sodium iodide to such patients was a disappointing 20%.

### DISCUSSION

DR. JOSEPH A. LUHAN: What danger is there in this method?

DR. THOMAS CRAIGMILE: As far as we know, there are no contraindications to the use of isotope study, and we have had no untoward effects.

DR. JOSEPH A. LUHAN: Is the radioactive material entirely eliminated within a short time?

DR. THOMAS CRAIGMILE: Yes. We have not been particularly troubled in the presence of intracranial tumors, later verified, by the fact that there is generally a higher uptake on the right side of the body than on the left, because of the presence of the liver. In midline tumors, particularly in the posterior fossa, we have probably produced increased radioactivity bilaterally except in the case of those superficially situated.

As to the criteria for what is normal and what is abnormal, usually an amplitude greater than 10% above our established standards has been regarded as an abnormal increase.

The question was asked concerning the size of a tumor that can be detected. I can say that no tumor that displayed no clinical evidence of its presence was discovered at operation and certainly, I think, not at autopsy. Only in very few instances was radioactive isotope study relied upon to determine whether or not operation should be done or where it should be done.

DR. R. P. MACKAY: Was the radioactive isotope examiner aware of the fact that the patient was suspected of having a tumor or aware of the clinical data already elicited?

DR. THOMAS CRAIGMILE: This question is an interesting and important one. In some cases, yes, he was aware; in others, he was not. I am sure our percentage of accuracy was higher when the isotope examiner was one who had examined the patients. I am certain that that factor would definitely influence the results of the study. In some instances he was the clinical examiner.



Douglas N. Buchanan, M.D., President

Meyer Brown, M.D., Secretary

Regular Meeting, March 9, 1954

The President announced the sudden death of the secretary, Dr. Leo Kaplan, on Feb. 20, 1954, and asked that the members stand in silence for one minute in fitting tribute to his memory. An obituary will be given at the April meeting.

**Cholesteatoma (Epidermoid) of the Spinal Cord.** DR. ERNEST T. AJAX (by invitation) and DR. JAMES J. DUFFY (by invitation).

An interesting case of cholesteatoma (epidermoid) of the spinal cord was presented.

Miss M. T., a 30-year-old laboratory technician with a prolonged history dating back to 1945, when she fell and injured her spine, was admitted to the neurosurgical service at Mercy Hospital Dec. 6, 1951. On one occasion she suffered a severe burn of her left foot without having any pain. Three years before she began to trip frequently when walking and noted progressive numbness involving her left foot. There was an insidious onset of urgency and frequency associated with progressive constipation.

Examination revealed moderate weakness in both lower extremities. The right Achilles reflex was diminished and the left Achilles reflex was absent. There was marked hypesthesia over the lower lumbar and sacral dermatomes. Myelography on Dec. 10, followed by laminectomy on Jan. 2, revealed a large intradural mass lying on the conus medullaris and among the lower roots of the cauda.

The subsequent course of the patient has been favorable, with some resolution of the weakness and bladder disturbance. She was transferred to the Veterans Administration Hospital, at Hines, Ill., for further rehabilitation.

A brief review of the scattered literature was given and the rarity of this type of tumor in the spinal canal emphasized.

#### DISCUSSION

DR. HAROLD C. VORIS: I anticipated that this tumor would recur because it was not completely removed. I have a patient, a little girl, the daughter of a physician, upon whom I have operated three times for cholesteatoma of the orbit. The tumor is grossly and microscopically exactly like this one. The last two operations were, of course, for recurrences. At every sitting the removal has been much more complete than in this case.

I have examined the authors' patient a number of times since operation, looking for any increase in neurological signs. So far the only change has been slow improvement, but no regression. A recurrence is eventually expected because the tumor was not removed, owing to the involvement of the conus medullaris.

DR. PERCIVAL BAILEY: I had one case somewhat similar to this except that the tumor was inside the spinal cord, in the upper thoracic region. It occurred in a professor at the University of Chicago, who came in complaining of atrophy of the deltoid muscles. We first thought it was secondary to arthritis of the shoulder. When he began to lose the use of his legs, we decided something else was wrong. We put in some iodized oil (Lipiodol) and found an obstruction in the upper thoracic region. We operated, and there was nothing to be seen except an enlarged spinal cord. We split the spinal cord in the midline and came down upon this tumor. I started to dissect it out; the capsule ruptured, and I spent the rest of my time digging it out with a spoon. We finally got it out, and there was not much left of the spinal cord. The patient made a good recovery, went back to his job, and had only a little stiffness in the legs. Five years later I operated on him a second time and took out the tumor, and seven years later I took it out for a third time. It is now 17 years since the last operation, and he has no sign of recurrence. He has had several lumbar punctures since then. The last time I operated it was impossible to see any spinal cord. He had an elevator installed in his house, and one day he fell into the shaft and injured his head. When I saw him, his head looked like an eggshell. I emptied out the blood clots and, except for a little hesitancy in speech, he recovered completely. Since his retirement from the University, he has published a learned treatise on animal ecology, has flown to Norway, has held another professorship, and last summer was married, at the age of 70.

**Stereotaxic Surgery.** DR. PERCIVAL BAILEY.

Electrolytic lesions in the interior of the brain were first made by means of insulated needles by Golsinger, at St. Petersburg, in 1895. Sellier and Verger, in 1898, used two needles bound together and insulated at their tips. The problem of exact placement of these needles was solved by R. H. Clarke by means of a stereotaxic instrument, often erroneously called a Horsley-Clarke instrument, although Horsley always referred to it as Clarke's stereotaxic instrument. This instrument, with its numerous modifications, has been extensively used to produce lesions in the brains of animals. Its purpose, of course, is to produce such lesions without injury to overlying structures.

It has long been desirable to have such an instrument for use on the human brain, but there are numerous difficulties to be overcome. Experimental instruments have been built by Gibbs and Hayne, Spiegel and Wycis, Taldirach, Lextell, Réymond, Bailey and Stein, and others. (A description of these instruments and an estimate of their virtues and defects were given, together with an account of the various neurological conditions for which they have been used.)

**Changes in Electroencephalographic Foci with Age.** DR. FREDERIC A. GIBBS.

Follow-up studies were carried out on 45 children who had passed their ninth birthday and who before the age of 9 had had an occipital lobe focus of seizure activity. Similar follow-up studies were carried out on 98 patients who had passed their 15th birthday and who before the age of 15 had had a mid-temporal-lobe focus. All the original electroencephalographic studies on these patients were made in both the waking and the sleeping states, and seizure foci had been found only in the areas specified. At the time of the follow-up studies electroencephalographic recordings were again obtained in both the waking and the sleeping states, for it was recognized that in a high percentage of cases epileptic disorder does not appear in the waking state.

Of the patients who had had occipital lobe epilepsy, 48% no longer had any evidence of disorder; i. e., their EEG's had entirely normalized after the age of 9 years. Of those who had had mid-temporal-lobe epilepsy, 50% no longer had any evidence of disorder; i. e., their EEG's had entirely normalized after the age of 15 years. Clinical seizures had ceased before the EEG became normal.

Present experience suggests that it is wise to continue anticonvulsant medication until one year after the last seizure in cases in which a previous abnormal EEG has become normal, while awake and asleep. Normalization of the EEG is evidence of a recovery process that probably has carried the patient out of danger of further seizures. In order to play doubly safe, however, medication can be continued for another year; a second normal EEG, while awake and asleep, at the end of that time indicates that no relapse has occurred and gives added assurance that medication can be discontinued without a recurrence of seizures.

Unless a tumor, abscess, depressed fracture, or other lesion which requires surgery is present, a neurosurgical attack on occipital and midtemporal foci in children is contraindicated.

DISCUSSION

DR. PERCIVAL BAILEY: One of the things we use the stereotaxic instrument for is to place electrodes in various parts of the brain to learn where the discharges are coming from so as to plan an operation. I have no explanation as to why these seizures stop at certain ages, but I know they can sometimes be abolished by operation, so it is well to have as much information as possible about the site of origin. Dr. Gibbs has devised a plan of placing multiple electrodes so as to locate the discharges, but he is not in position to report on it yet. I simply want to point out that this is another purpose for which the stereotaxic instrument can be used.

DR. RAY SNYDER: Does this shifting take place whether or not these children are on medication?

DR. FREDERIC A. GIBBS: All of our patients have been on treatment with at least one anticonvulsant drug, and many have been on treatment with several drugs simultaneously. We do not know what would happen if our patients were not on medication.

Of course, Dr. Bailey is right; we shall learn much more about the spread of epileptic disorder and the origin of epileptic discharges when we can put needle electrodes into various

subcortical structures. Dr. John Kendrick is doing this at the Manteno State Hospital in an effort to delimit more sharply the anterior temporal lobe focus of psychomotor epilepsy. So far, he has not used Dr. Bailey's stereotaxic instrument, but the stereotaxic technique which Dr. Bailey and Dr. Amador are developing will be invaluable in later phases of this and similar work.

No one has asked specifically whether occipital and midtemporal epileptic foci result from localized seizure discharges in these areas, or whether the discharge originates in some deeper center and spreads to these particular cortical areas. We have no positive evidence on this point, but we have impressions based on a considerable experience with focal discharges. It is our belief that the sharply localized, high-voltage spike foci which we see in the occipital and midtemporal regions are primarily occipital and temporal and do not come from the central gray masses of distant parts of the brain.

## Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

### Anatomy and Embryology

**ANATOMICAL CONSIDERATIONS IN THE PATHOLOGY OF STENOSIS OF THE CEREBRAL AQUEDUCT.**  
D. H. M. WOOLLAM and J. W. MILLEN, *Brain* **76**:104 (March) 1953.

Woollam and Millen's objective is to provide more detailed information than has been hitherto available upon the anatomy of the cerebral aqueduct, in relation to landmarks in the surface of the midbrain and the normal variations in its dimensions.

The authors take the cranial limit as the level (perpendicular to the long axis of the brain stem) immediately caudal to the posterior commissure, and the caudal limit as the level immediately caudal to the inferior colliculus; therefore, the aqueduct is that part of the ventricular system lying ventral to the tectum.

There are two constrictions, one at the level of the middle of the superior colliculus and the other at the level of the intercollicular sulcus. At the latter the lumen is reduced to its smallest average dimension. Between the constrictions the lumen dilates to form the ampulla, the area of greatest dimensions. The authors suggest the terms *pars anterior*, *ampulla*, and *pars posterior*. In transverse sections the shape of the aqueduct varies at different levels, perhaps owing to the developmental influence of surrounding nuclear masses and fiber tracts. The average length of the aqueduct is 11 mm. (7 to 12 mm.); the area of cross section of the ampulla is 1.8 sq. mm. (0.8 to 2.9 sq. mm.); the area of cross section at the lower end of the ampulla is 0.8 sq. mm. (0.4 to 1.5 sq. mm.). It is believed that the length of the aqueduct varies inversely as its mean area of cross section varies.

The authors raise the question as to whether the present views of the method of formation and rate of circulation of the cerebrospinal fluid should not be reconsidered in the light of the minute dimensions of the aqueduct. They discuss at length the bearing of their information upon the various theories of, and reports of pathology in, hydrocephalus.

JOHNS, New York.

### Physiology and Biochemistry

**STUDY OF THALAMIC AND CORTICAL RHYTHMS IN PETIT MAL.** D. WILLIAMS, *Brain* **76**:50 (March) 1953.

Williams presents his fascinating work in which electroencephalographic records were obtained from the thalamus, white matter, and cerebral cortex during true petit mal seizures in children. Only six children with a large number of seizures were studied, as the prerequisites were sufficiently frequent petit mal attacks, typical rhythmic 3-per-second wave and spike discharges on EEG, and ventriculography, which was necessary for reasonably accurate placement of the coaxial electrodes.

The sequence of events in the petit mal attack was found to be as follows: A rhythm of 3 per second begins deep in the thalamus. It increases in voltage and persistence until it reaches the cortex, at which time a fast spike originates deep in the cortex. The "initial spike" usually has a high voltage and travels down to the thalamus, either directly or via more superficial layers of the cortex. As the spike reaches the thalamus, the site of origin of the 3-per-second wave alters and becomes more superficial (lateral and ventral) within the thalamus. The wave which arises in the new position in the thalamus is then followed by a spike arising from deep in the cortex, etc. As the attack proceeds, the rate usually slows to 2.5 per second, and the voltage of the cortical spike drops, then ceases. The wave then disappears. Although the thalamic rhythm seems to be responsible for the cortical spike, the latter seems to be essential for continuation of the 3-per-second rhythm; if the wave recommences and no spike occurs, the rhythm is not sustained. If the rhythm does not recur in a constant position deep in the thalamus, it does not develop a cortical spike, the rhythm dies, and the attack is aborted.

Williams advances the hypothesis that petit mal attacks are due to a disturbance in the thalamus which causes a rhythmic discharge throughout the cortex. Petit mal may be regarded as a periodic disorganization of the afferent, effector side of the organism, which inhibits all

awareness and "spontaneous" behavior, in contrast to other forms of epilepsy, in which the disorganization may be considered to occur in the effector mechanisms.

It should be noted that this study is the first work of this nature in humans.

JOHNS, New York.

**METABOLISM IN PARAPLEGIA.** F. B. O'CONNELL JR. and W. J. GARDNER, J. A. M. A. **153**:706 (Oct. 24) 1953.

The present knowledge of metabolic changes in paraplegia is presented by O'Connell and Gardner. Many of these changes are not limited to the paraplegic patient but occur as definite and consistent reactions to trauma of any form.

The effects of the immobilization and bed rest are discussed, and the changes occurring in paraplegic patients in protein, electrolyte, calcium and phosphorus, and hormone metabolism are presented.

Some specific complications of paraplegia are discussed, with emphasis on the metabolic abnormalities that underlie them. Decubitus ulcer is a common complication and is due to local tissue changes, in addition to the factors of protein depletion and anemia. Anemia and hypoproteinemia often are the two most evident clinical manifestations of serious metabolic alterations in the paraplegic patient.

Some degree of liver function impairment is a consequence of trauma and is particularly noted after spinal cord transections. The mechanism of impairment of liver function is indefinite, but it appears to be one of the many organ changes of the post-traumatic catabolism.

The paraplegic patient frequently has abnormal changes in the bones or the adjacent soft tissues in the paralyzed portion of the body. These changes are caused partly by abnormal local stimuli or the lack of stimulation and partly by the body's response to abnormal metabolic changes. The effect of ambulation on these abnormal bone and soft tissue changes is profound, definitely keeping them to a minimal degree.

The genitourinary tract is particularly susceptible to pathological alterations. The most important metabolic changes that affect the genitourinary tract are those of calcium and phosphorus content. The incidence of renal calculi in spinal cord injuries of all types varies from 10 to 20%, and that of bladder calculi, from 20 to 70%. Of the various methods of diminishing the concentration of calcium in the urine, the best prophylaxis is ambulation, which decreases the hypercalcinuria almost immediately.

Hormonal changes, which are an integral part of the body's response to the trauma of spinal cord transection, may have some profound effects upon the various endocrine systems and sexual functions of the body. In a series of paraplegic men, studied by Cooper, testicular atrophy occurred in over 50%. Gynecomastia has been observed in 22 to 25% of paraplegic men. Menses are usually scant or cease in the few young adult women seen with post-traumatic paraplegia.

ALPERS, Philadelphia.

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## News and Comment

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### AMERICAN ACADEMY FOR CEREBRAL PALSY

The Eighth Annual Meeting of the American Academy for Cerebral Palsy will be held on Nov. 4, 5, and 6, 1954, in Williamsburg, Va., at the Williamsburg Inn.

### THE AMERICAN NEUROLOGICAL ASSOCIATION

At the 79th Annual Meeting of The American Neurological Association, held in Atlantic City, N. J., from June 14-16, 1954, the following officers were elected for the year 1954-1955: president, Dr. Percival Bailey; president-elect, Dr. J. M. Nielsen; first vice-president, Dr. A. R. Vonderahe; second vice-president, Dr. Paul C. Bucy; secretary-treasurer, Dr. H. Houston Merritt, and assistant secretary, Dr. Charles Rupp.

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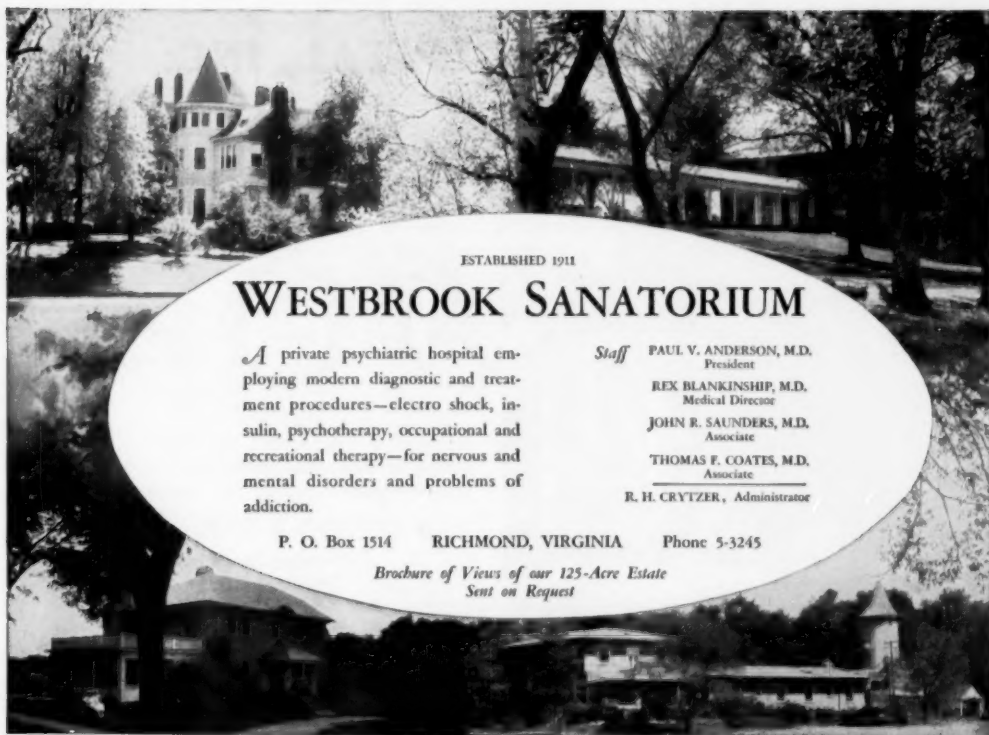
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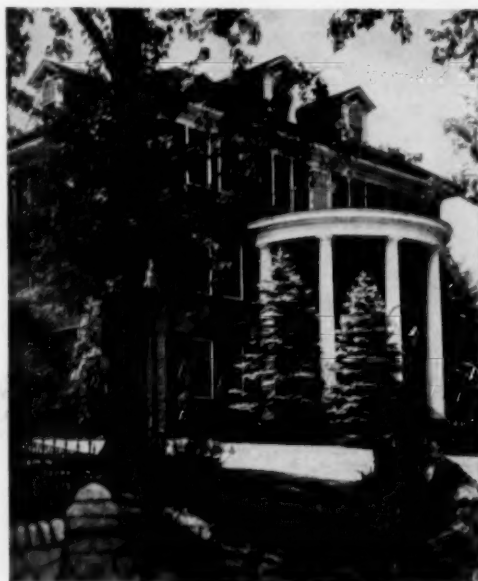
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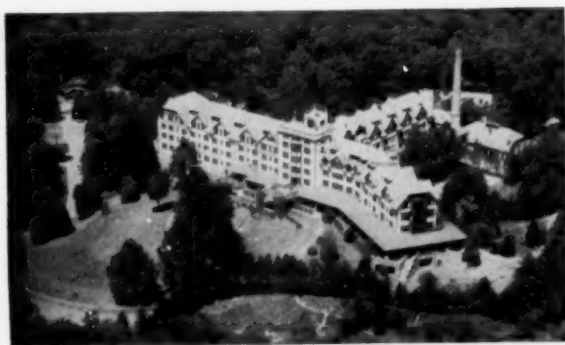
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